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(54) Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amine acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57

(57) Abstract: The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.



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SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

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BACKGROUND OF THE INVENTION

Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci. 93:7108-7113 (1996); U.S. Patent No. 5,536,637)].

Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesin molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and

nerve growth factor receptor.

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Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

SUMMARY OF THE INVENTION

In one embodiment, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.

In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93 % nucleic acid sequence identity, alternatively at least about 94 % nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 94%

nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 99% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complement thereof, that may find use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleic acid fragments are usually at least about 10 nucleotides in length, alternatively at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length,

alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160 nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 900 nucleotides in length and alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

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In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid

sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein.

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In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as hereinbefore described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof as hereinbefore described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

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In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

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In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a Fc region of an immunoglobulin.

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In another embodiment, the invention provides an antibody which binds, preferably specifically, to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.

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In yet other embodiments, the invention provides oligonucleotide probes which may be useful for isolating genomic and cDNA nucleotide sequences, measuring or detecting expression of an associated gene or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences. Preferred probe lengths are described above.

In yet other embodiments, the present invention is directed to methods of using the PRO polypeptides of the present invention for a variety of uses based upon the functional biological assay data presented in the Examples below.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO177 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA16438-1387".

Figure 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in Figure 1.

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Figure 3 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO3574 cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA19360-2552".

Figure 4 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in Figure 3.

NO:3 snown in Figure 3.

Figure 5 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO1280 cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA33455-1548".

Figure 6 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in Figure 5.

Figure 7 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO4984 cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA37155-2651".

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Figure 8 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in Figure 7.

Figure 9 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO4988 cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA38269-2654".

Figure 10 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in Figure 9.

Figure 11 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO305 cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA40619-1220".

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Figure 12 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in Figure 11.

Figure 13 shows a nucleotide sequence (SEQ ID NO:13) of a native sequence PRO1866 cDNA, wherein SEQ ID NO:13 is a clone designated herein as "DNA44174-2513".

Figure 14 shows the amino acid sequence (SEQ ID NO:14) derived from the coding sequence of SEQ ID NO:13 shown in Figure 13.

Figure 15 shows a nucleotide sequence (SEQ ID NO:15) of a native sequence PRO4996 cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA44675-2662".

Figure 16 shows the amino acid sequence (SEQ ID NO:16) derived from the coding sequence of SEQ ID NO:15 shown in Figure 15.

Figure 17 shows a nucleotide sequence (SEQ ID NO:17) of a native sequence PRO4406 cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA45408-2615".

Figure 18 shows the amino acid sequence (SEQ ID NO:18) derived from the coding sequence of SEQ ID NO:17 shown in Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO:19) of a native sequence PRO1120 cDNA, wherein SEQ ID NO:19 is a clone designated herein as "DNA48606-1479".

Figure 20 shows the amino acid sequence (SEQ ID NO:20) derived from the coding sequence of SEQ ID NO:19 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO4990 cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA52753-2656".

Figure 22 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in Figure 21.

Figure 23 shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO738 cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA53915-1258".

Figure 24 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in Figure 23.

Figure 25 shows a nucleotide sequence (SEQ ID NO:25) of a native sequence PRO3577 cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA53991-2553".

Figure 26 shows the amino acid sequence (SEQ ID NO:26) derived from the coding sequence of SEQ ID NO:25 shown in Figure 25.

Figure 27 shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO1879 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA54009-2517".

Figure 28 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in Figure 27.

Figure 29 shows a nucleotide sequence (SEQ ID NO:29) of a native sequence PRO1471 cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA56055-1643".

Figure 30 shows the amino acid sequence (SEQ ID NO:30) derived from the coding sequence of SEQ ID NO:29 shown in Figure 29.

Figure 31 shows a nucleotide sequence (SEQ ID NO:31) of a native sequence PRO1114 cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA57033-1403".

Figure 32 shows the amino acid sequence (SEQ ID NO:32) derived from the coding sequence of SEQ ID NO:31 shown in Figure 31.

Figure 33 shows a nucleotide sequence (SEQ ID NO:33) of a native sequence PRO1076 cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA57252-1453".

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Figure 34 shows the amino acid sequence (SEQ ID NO:34) derived from the coding sequence of SEQ ID NO:33 shown in Figure 33.

Figure 35 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO1483 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA58799-1652".

Figure 36 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of SEQ ID NO:35 shown in Figure 35.

Figure 37 shows a nucleotide sequence (SEQ ID NO:37) of a native sequence PRO4985 cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA59770-2652".

Figure 38 shows the amino acid sequence (SEQ ID NO:38) derived from the coding sequence of SEQ ID NO:37 shown in Figure 37.

Figure 39 shows a nucleotide sequence (SEQ ID NO:39) of a native sequence PRO5000 cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA59774-2665".

Figure 40 shows the amino acid sequence (SEQ ID NO:40) derived from the coding sequence of SEQ ID NO:39 shown in Figure 39.

Figure 41 shows a nucleotide sequence (SEQ ID NO:41) of a native sequence PRO1881 cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA60281-2518".

Figure 42 shows the amino acid sequence (SEQ ID NO:42) derived from the coding sequence of SEQ ID NO:41 shown in Figure 41.

Figure 43 shows a nucleotide sequence (SEQ ID NO:43) of a native sequence PRO4314 cDNA, wherein SEQ ID NO:43 is a clone designated herein as "DNA60736-2559".

Figure 44 shows the amino acid sequence (SEQ ID NO:44) derived from the coding sequence of SEQ ID NO:43 shown in Figure 43.

Figure 45 shows a nucleotide sequence (SEQ ID NO:45) of a native sequence PRO4987 cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA61875-2653".

Figure 46 shows the amino acid sequence (SEQ ID NO:46) derived from the coding sequence of SEQ ID NO:45 shown in Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO:47) of a native sequence PRO4313 cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA62312-2558".

Figure 48 shows the amino acid sequence (SEQ ID NO:48) derived from the coding sequence of SEQ ID NO:47 shown in Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO4799 cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA62849-1604".

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Figure 50 shows the amino acid sequence (SEQ ID NO:50) derived from the coding sequence of SEQ ID NO:49 shown in Figure 49.

Figure 51 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO4995 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA66307-2661".

Figure 52 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in Figure 51.

Figure 53 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO1341 cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA66677-2535".

Figure 54 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in Figure 53.

Figure 55 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1777 cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA71235-1706".

Figure 56 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of SEQ ID NO:55 shown in Figure 55.

Figure 57 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO3580 cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA71289-2547".

Figure 58 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO:59) of a native sequence PRO1779 cDNA, wherein SEQ ID NO:59 is a clone designated herein as "DNA73775-1707".

Figure 60 shows the amino acid sequence (SEQ ID NO:60) derived from the coding sequence of SEQ ID NO:59 shown in Figure 59.

Figure 61 shows a nucleotide sequence (SEQ ID NO:61) of a native sequence PRO1754 cDNA, wherein SEQ ID NO:61 is a clone designated herein as "DNA76385-1692".

Figure 62 shows the amino acid sequence (SEQ ID NO:62) derived from the coding sequence of SEQ ID NO:61 shown in Figure 61.

Figure 63 shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO1906 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "DNA76395-2527".

Figure 64 shows the amino acid sequence (SEQ ID NO:64) derived from the coding sequence of SEQ ID NO:63 shown in Figure 63.

Figure 65 shows a nucleotide sequence (SEQ ID NO:65) of a native sequence PRO1870 cDNA, wherein SEQ ID NO:65 is a clone designated herein as "DNA77622-2516".

Figure 66 shows the amino acid sequence (SEQ ID NO:66) derived from the coding sequence of SEQ ID NO:65 shown in Figure 65.

Figure 67 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO4329 cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA77629-2573".

Figure 68 shows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 shown in Figure 67.

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Figure 69 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO4979 cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA77645-2648".

Figure 70 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in Figure 69.

Figure 71 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1885 cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA79302-2521".

Figure 72 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in Figure 71.

Figure 73 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO1882 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "DNA79865-2519".

Figure 74 shows the amino acid sequence (SEQ ID NO:74) derived from the coding sequence of SEQ ID NO:73 shown in Figure 73.

Figure 75 shows a nucleotide sequence (SEQ ID NO:75) of a native sequence PRO4989 cDNA, wherein SEQ ID NO:75 is a clone designated herein as "DNA80135-2655".

Figure 76 shows the amino acid sequence (SEQ ID NO:76) derived from the coding sequence of SEQ ID NO:75 shown in Figure 75.

Figure 77 shows a nucleotide sequence (SEQ ID NO:77) of a native sequence PRO4323 cDNA, wherein SEQ ID NO:77 is a clone designated herein as "DNA80794-2568".

Figure 78 shows the amino acid sequence (SEQ ID NO:78) derived from the coding sequence of SEQ ID NO:77 shown in Figure 77.

Figure 79 shows a nucleotide sequence (SEQ ID NO:79) of a native sequence PRO1886 cDNA, wherein SEQ ID NO:79 is a clone designated herein as "DNA80796-2523".

Figure 80 shows the amino acid sequence (SEQ ID NO:80) derived from the coding sequence of SEQ ID NO:79 shown in Figure 79.

Figure 81 shows a nucleotide sequence (SEQ ID NO:81) of a native sequence PRO4395 cDNA, wherein SEQ ID NO:81 is a clone designated herein as "DNA80840-2605".

Figure 82 shows the amino acid sequence (SEQ ID NO:82) derived from the coding sequence of SEQ ID NO:81 shown in Figure 81.

Figure 83 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO1782 cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA80899-2501".

Figure 84 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in Figure 83.

Figure 85 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO4338 cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA81228-2580".

Figure 86 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO4341 cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA81761-2583".

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Figure 88 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in Figure 87.

Figure 89 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO5990 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "DNA96042-2682".

Figure 90 shows the amino acid sequence (SEQ ID NO:90) derived from the coding sequence of SEQ ID NO:89 shown in Figure 89.

Figure 91 shows a nucleotide sequence (SEQ ID NO:91) of a native sequence PRO3438 cDNA, wherein SEQ ID NO:91 is a clone designated herein as "DNA82364-2538".

Figure 92 shows the amino acid sequence (SEQ ID NO:92) derived from the coding sequence of SEQ ID NO:91 shown in Figure 91.

Figure 93 shows a nucleotide sequence (SEQ ID NO:93) of a native sequence PRO4321 cDNA, wherein SEQ ID NO:93 is a clone designated herein as "DNA82424-2566".

Figure 94 shows the amino acid sequence (SEQ ID NO:94) derived from the coding sequence of SEQ ID NO:93 shown in Figure 93.

Figure 95 shows a nucleotide sequence (SEQ ID NO:95) of a native sequence PRO4304 cDNA, wherein SEQ ID NO:95 is a clone designated herein as "DNA82430-2557".

Figure 96 shows the amino acid sequence (SEQ ID NO:96) derived from the coding sequence of SEQ ID NO:95 shown in Figure 95.

Figure 97 shows a nucleotide sequence (SEQ ID NO:97) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:97 is a clone designated herein as "DNA83500-2506".

Figure 98 shows the amino acid sequence (SEQ ID NO:98) derived from the coding sequence of SEQ ID NO:97 shown in Figure 97.

Figure 99 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO4403 cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA83509-2612".

Figure 100 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in Figure 99.

Figure 101 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO4324 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA83560-2569".

Figure 102 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:101 shown in Figure 101.

Figure 103 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO4303 cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA84139-2555".

Figure 104 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in Figure 103.

Figure 105 shows a nucleotide sequence (SEQ ID NO:105) of a native sequence PRO4305 cDNA, wherein SEQ ID NO:105 is a clone designated herein as "DNA84141-2556".

Figure 106 shows the amino acid sequence (SEQ ID NO:106) derived from the coding sequence of SEQ ID NO:105 shown in Figure 105.

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Figure 107 shows a nucleotide sequence (SEQ ID NO:107) of a native sequence PRO4404 cDNA, wherein SEQ ID NO:107 is a clone designated herein as "DNA84142-2613".

Figure 108 shows the amino acid sequence (SEQ ID NO:108) derived from the coding sequence of SEQ ID NO:107 shown in Figure 107.

Figure 109 shows a nucleotide sequence (SEQ ID NO:109) of a native sequence PRO1884 cDNA, wherein SEQ ID NO:109 is a clone designated herein as "DNA84318-2520".

Figure 110 shows the amino acid sequence (SEQ ID NO:110) derived from the coding sequence of SEQ ID NO:109 shown in Figure 109.

Figure 111 shows a nucleotide sequence (SEQ ID NO:111) of a native sequence PRO4349 cDNA, wherein SEQ ID NO:111 is a clone designated herein as "DNA84909-2590".

Figure 112 shows the amino acid sequence (SEQ ID NO:112) derived from the coding sequence of SEQ ID NO:111 shown in Figure 111.

Figure 113 shows a nucleotide sequence (SEQ ID NO:113) of a native sequence PRO4401 cDNA, wherein SEQ ID NO:113 is a clone designated herein as "DNA84912-2610".

Figure 114 shows the amino acid sequence (SEQ ID NO:114) derived from the coding sequence of SEQ ID NO:113 shown in Figure 113.

Figure 115 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1867 cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA84925-2514".

Figure 116 shows the amino acid sequence (SEQ ID NO:116) derived from the coding sequence of SEQ ID NO:115 shown in Figure 115.

Figure 117 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO4319 cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA84928-2564".

Figure 118 shows the amino acid sequence (SEQ ID NO:118) derived from the coding sequence of SEQ ID NO:117 shown in Figure 117.

Figure 119 shows a nucleotide sequence (SEQ ID NO:119) of a native sequence PRO4991 cDNA, wherein SEQ ID NO:119 is a clone designated herein as "DNA84932-2657".

Figure 120 shows the amino acid sequence (SEQ ID NO:120) derived from the coding sequence of SEQ ID NO:119 shown in Figure 119.

Figure 121 shows a nucleotide sequence (SEQ ID NO:121) of a native sequence PRO4398 cDNA, wherein SEQ ID NO:121 is a clone designated herein as "DNA86592-2607".

Figure 122 shows the amino acid sequence (SEQ ID NO:122) derived from the coding sequence of SEQ ID NO:121 shown in Figure 121.

Figure 123 shows a nucleotide sequence (SEQ ID NO:123) of a native sequence PRO4346 cDNA, wherein SEQ ID NO:123 is a clone designated herein as "DNA86594-2587".

Figure 124 shows the amino acid sequence (SEQ ID NO:124) derived from the coding sequence of SEQ ID NO:123 shown in Figure 123.

Figure 125 shows a nucleotide sequence (SEQ ID NO:125) of a native sequence PRO4350 cDNA, wherein SEQ ID NO:125 is a clone designated herein as "DNA86647-2591".

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Figure 126 shows the amino acid sequence (SEQ ID NO:126) derived from the coding sequence of SEQ ID NO:125 shown in Figure 125.

Figure 127 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO4318 cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA87185-2563".

Figure 128 shows the amino acid sequence (SEQ ID NO:128) derived from the coding sequence of SEQ ID NO:127 shown in Figure 127.

Figure 129 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO4340 cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA87656-2582".

Figure 130 shows the amino acid sequence (SEQ ID NO:130) derived from the coding sequence of SEQ ID NO:129 shown in Figure 129.

Figure 131 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO4400 cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA87974-2609".

Figure 132 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in Figure 131.

Figure 133 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO4320 cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA88001-2565".

Figure 134 shows the amino acid sequence (SEQ ID NO:134) derived from the coding sequence of SEQ ID NO:133 shown in Figure 133.

Figure 135 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO4409 cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA88004-2575".

Figure 136 shows the amino acid sequence (SEQ ID NO:136) derived from the coding sequence of SEQ ID NO:135 shown in Figure 135.

Figure 137 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO4399 cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA89220-2608".

Figure 138 shows the amino acid sequence (SEQ ID NO:138) derived from the coding sequence of SEQ ID NO:137 shown in Figure 137.

Figure 139 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO4418 cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA89947-2618".

Figure 140 shows the amino acid sequence (SEQ ID NO:140) derived from the coding sequence of SEQ ID NO:139 shown in Figure 139.

Figure 141 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO4330 cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA90842-2574".

Figure 142 shows the amino acid sequence (SEQ ID NO:142) derived from the coding sequence of SEQ ID NO:141 shown in Figure 141.

Figure 143 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO4339 cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA91775-2581".

Figure 144 shows the amino acid sequence (SEQ ID NO:144) derived from the coding sequence of SEQ ID NO:143 shown in Figure 143.

Figure 145 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO4326 cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA91779-2571".

Figure 146 shows the amino acid sequence (SEQ ID NO:146) derived from the coding sequence of SEQ ID NO:145 shown in Figure 145.

Figure 147 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO6014 cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA92217-2697".

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Figure 148 shows the amino acid sequence (SEQ ID NO:148) derived from the coding sequence of SEQ ID NO:147 shown in Figure 147.

Figure 149 shows a nucleotide sequence (SEQ ID NO:149) of a native sequence PRO3446 cDNA, wherein SEQ ID NO:149 is a clone designated herein as "DNA92219-2541".

Figure 150 shows the amino acid sequence (SEQ ID NO:150) derived from the coding sequence of SEQ ID NO:149 shown in Figure 149.

Figure 151 shows a nucleotide sequence (SEQ ID NO:151) of a native sequence PRO4322 cDNA, wherein SEQ ID NO:151 is a clone designated herein as "DNA92223-2567".

Figure 152 shows the amino acid sequence (SEQ ID NO:152) derived from the coding sequence of SEQ ID NO:151 shown in Figure 151.

Figure 153 shows a nucleotide sequence (SEQ ID NO:153) of a native sequence PRO4381 cDNA, wherein SEQ ID NO:153 is a clone designated herein as "DNA92225-2603".

Figure 154 shows the amino acid sequence (SEQ ID NO:154) derived from the coding sequence of SEQ ID NO:153 shown in Figure 153.

Figure 155 shows a nucleotide sequence (SEQ ID NO:155) of a native sequence PRO4348 cDNA, wherein SEQ ID NO:155 is a clone designated herein as "DNA92232-2589".

Figure 156 shows the amino acid sequence (SEQ ID NO:156) derived from the coding sequence of SEQ ID NO:155 shown in Figure 155.

Figure 157 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO4371 cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA92233-2599".

Figure 158 shows the amino acid sequence (SEQ ID NO:158) derived from the coding sequence of SEQ ID NO:157 shown in Figure 157.

Figure 159 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO3742 cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA92243-2549".

Figure 160 shows the amino acid sequence (SEQ ID NO:160) derived from the coding sequence of SEQ ID NO:159 shown in Figure 159.

Figure 161 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO5773 cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA92253-2671".

Figure 162 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ ID NO:161 shown in Figure 161.

Figure 163 shows a nucleotide sequence (SEQ ID NO:163) of a native sequence PRO5774 cDNA, wherein SEQ ID NO:163 is a clone designated herein as "DNA92254-2672".

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Figure 164 shows the amino acid sequence (SEQ ID NO:164) derived from the coding sequence of SEQ ID NO:163 shown in Figure 163.

Figure 165 shows a nucleotide sequence (SEQ ID NO:165) of a native sequence PRO4343 cDNA, wherein SEQ ID NO:165 is a clone designated herein as "DNA92255-2584".

Figure 166 shows the amino acid sequence (SEQ ID NO:166) derived from the coding sequence of SEQ ID NO:165 shown in Figure 165.

Figure 167 shows a nucleotide sequence (SEQ ID NO:167) of a native sequence PRO4325 cDNA, wherein SEQ ID NO:167 is a clone designated herein as "DNA92269-2570".

Figure 168 shows the amino acid sequence (SEQ ID NO:168) derived from the coding sequence of SEQ ID NO:167 shown in Figure 167.

Figure 169 shows a nucleotide sequence (SEQ ID NO:169) of a native sequence PRO4347 cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA92288-2588".

Figure 170 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ ID NO:169 shown in Figure 169.

Figure 171 shows a nucleotide sequence (SEQ ID NO:171) of a native sequence PRO3743 cDNA, wherein SEQ ID NO:171 is a clone designated herein as "DNA92290-2550".

Figure 172 shows the amino acid sequence (SEQ ID NO:172) derived from the coding sequence of SEQ ID NO:171 shown in Figure 171.

Figure 173 shows a nucleotide sequence (SEQ ID NO:173) of a native sequence PRO4426 cDNA, wherein SEQ ID NO:173 is a clone designated herein as "DNA93012-2622".

Figure 174 shows the amino acid sequence (SEQ ID NO:174) derived from the coding sequence of SEQ ID NO:173 shown in Figure 173.

Figure 175 shows a nucleotide sequence (SEQ ID NO:175) of a native sequence PRO4500 cDNA, wherein SEQ ID NO:175 is a clone designated herein as "DNA93020-2642".

Figure 176 shows the amino acid sequence (SEQ ID NO:176) derived from the coding sequence of SEQ ID NO:175 shown in Figure 175.

Figure 177 shows a nucleotide sequence (SEQ ID NO:177) of a native sequence PRO4389 cDNA, wherein SEQ ID NO:177 is a clone designated herein as "DNA94830-2604".

Figure 178 shows the amino acid sequence (SEQ ID NO:178) derived from the coding sequence of SEQ ID NO:177 shown in Figure 177.

Figure 179 shows a nucleotide sequence (SEQ ID NO:179) of a native sequence PRO4337 cDNA, wherein SEQ ID NO:179 is a clone designated herein as "DNA94833-2579".

Figure 180 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ ID NO:179 shown in Figure 179.

Figure 181 shows a nucleotide sequence (SEQ ID NO:181) of a native sequence PRO4992 cDNA, wherein SEQ ID NO:181 is a clone designated herein as "DNA94838-2658".

Figure 182 shows the amino acid sequence (SEQ ID NO:182) derived from the coding sequence of SEQ ID NO:181 shown in Figure 181.

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Figure 183 shows a nucleotide sequence (SEQ ID NO:183) of a native sequence PRO5996 cDNA, wherein SEQ ID NO:183 is a clone designated herein as "DNA94844-2686".

Figure 184 shows the amino acid sequence (SEQ ID NO:184) derived from the coding sequence of SEQ ID NO:183 shown in Figure 183.

Figure 185 shows a nucleotide sequence (SEQ ID NO:185) of a native sequence PRO4345 cDNA, wherein SEQ ID NO:185 is a clone designated herein as "DNA94854-2586".

Figure 186 shows the amino acid sequence (SEQ ID NO:186) derived from the coding sequence of SEQ ID NO:185 shown in Figure 185.

Figure 187 shows a nucleotide sequence (SEQ ID NO:187) of a native sequence PRO4978 cDNA, wherein SEQ ID NO:187 is a clone designated herein as "DNA95930".

Figure 188 shows the amino acid sequence (SEQ ID NO:188) derived from the coding sequence of SEQ ID NO:187 shown in Figure 187.

Figure 189 shows a nucleotide sequence (SEQ ID NO:189) of a native sequence PRO5780 cDNA, wherein SEQ ID NO:189 is a clone designated herein as "DNA96868-2677".

Figure 190 shows the amino acid sequence (SEQ ID NO:190) derived from the coding sequence of SEQ ID NO:189 shown in Figure 189.

Figure 191 shows a nucleotide sequence (SEQ ID NO:191) of a native sequence PRO5992 cDNA, wherein SEQ ID NO:191 is a clone designated herein as "DNA96871-2683".

Figure 192 shows the amino acid sequence (SEQ ID NO:192) derived from the coding sequence of SEQ ID NO:191 shown in Figure 191.

Figure 193 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO4428 cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA96880-2624".

Figure 194 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO4994 cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA96986-2660".

Figure 196 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO5995 cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA96988-2685".

Figure 198 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:197 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:199) of a native sequence PRO6094 cDNA, wherein SEQ ID NO:199 is a clone designated herein as "DNA96995-2709".

Figure 200 shows the amino acid sequence (SEQ ID NO:200) derived from the coding sequence of SEQ ID NO:199 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:201) of a native sequence PRO4317 cDNA, wherein SEQ ID NO:201 is a clone designated herein as "DNA97004-2562".

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Figure 202 shows the amino acid sequence (SEQ ID NO:202) derived from the coding sequence of SEQ ID NO:201 shown in Figure 201.

Figure 203 shows a nucleotide sequence (SEQ ID NO:203) of a native sequence PRO5997 cDNA, wherein SEQ ID NO:203 is a clone designated herein as "DNA97005-2687".

Figure 204 shows the amino acid sequence (SEQ ID NO:204) derived from the coding sequence of SEQ ID NO:203 shown in Figure 203.

Figure 205 shows a nucleotide sequence (SEQ ID NO:205) of a native sequence PRO5005 cDNA, wherein SEQ ID NO:205 is a clone designated herein as "DNA97009-2668".

Figure 206 shows the amino acid sequence (SEQ ID NO:206) derived from the coding sequence of SEQ ID NO:205 shown in Figure 205.

Figure 207 shows a nucleotide sequence (SEQ ID NO:207) of a native sequence PRO5004 cDNA, wherein SEQ ID NO:207 is a clone designated herein as "DNA97013-2667".

Figure 208 shows the amino acid sequence (SEQ ID NO:208) derived from the coding sequence of SEQ ID NO:207 shown in Figure 207.

Figure 209 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO6001 cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA98380-2690".

Figure 210 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in Figure 209.

Figure 211 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO6013 cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA98561-2696".

Figure 212 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in Figure 211.

Figure 213 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO4502 cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA98575-2644".

Figure 214 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in Figure 213.

Figure 215 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO6007 cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA98593-2694".

Figure 216 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 215.

Figure 217 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO6028 cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA98600-2703".

Figure 218 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 217.

Figure 219 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence PRO100 cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA99333".

Figure 220 shows the amino acid sequence (SEQ ID NO:220) derived from the coding sequence of SEQ ID NO:219 shown in Figure 219.

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Figure 221 shows a nucleotide sequence (SEQ ID NO:221) of a native sequence PRO4327 cDNA, wherein SEQ ID NO:221 is a clone designated herein as "DNA99391-2572".

Figure 222 shows the amino acid sequence (SEQ ID NO:222) derived from the coding sequence of SEQ ID NO:221 shown in Figure 221.

Figure 223 shows a nucleotide sequence (SEQ ID NO:223) of a native sequence PRO4315 cDNA, wherein SEQ ID NO:223 is a clone designated herein as "DNA99393-2560".

Figure 224 shows the amino acid sequence (SEQ ID NO:224) derived from the coding sequence of SEQ ID NO:223 shown in Figure 223.

Figure 225 shows a nucleotide sequence (SEQ ID NO:225) of a native sequence PRO5993 cDNA, wherein SEQ ID NO:225 is a clone designated herein as "DNA100276-2684".

Figure 226 shows the amino acid sequence (SEQ ID NO:226) derived from the coding sequence of SEQ ID NO:225 shown in Figure 225.

Figure 227 shows a nucleotide sequence (SEQ ID NO:227) of a native sequence PRO4503 cDNA, wherein SEQ ID NO:227 is a clone designated herein as "DNA100312-2645".

Figure 228 shows the amino acid sequence (SEQ ID NO:228) derived from the coding sequence of SEQ ID NO:227 shown in Figure 227.

Figure 229 shows a nucleotide sequence (SEQ ID NO:229) of a native sequence PRO4976 cDNA, wherein SEQ ID NO:229 is a clone designated herein as "DNA100902-2646".

Figure 230 shows the amino acid sequence (SEQ ID NO:230) derived from the coding sequence of SEQ ID NO:229 shown in Figure 229.

Figure 231 shows a nucleotide sequence (SEQ ID NO:231) of a native sequence PRO5798 cDNA, wherein SEQ ID NO:231 is a clone designated herein as "DNA102899-2679".

Figure 232 shows the amino acid sequence (SEQ ID NO:232) derived from the coding sequence of SEQ ID NO:231 shown in Figure 231.

Figure 233 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO6242 cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA104875-2720".

Figure 234 shows the amino acid sequence (SEQ ID NO:234) derived from the coding sequence of SEQ ID NO:233 shown in Figure 233.

Figure 235 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO6095 cDNA, wherein SEQ ID NO:235 is a clone designated herein as "DNA105680-2710".

Figure 236 shows the amino acid sequence (SEQ ID NO:236) derived from the coding sequence of SEQ ID NO:235 shown in Figure 235.

Figure 237 shows a nucleotide sequence (SEQ ID NO:237) of a native sequence PRO6093 cDNA, wherein SEQ ID NO:237 is a clone designated herein as "DNA105779-2708".

Figure 238 shows the amino acid sequence (SEQ ID NO:238) derived from the coding sequence of SEQ ID NO:237 shown in Figure 237.

Figure 239 shows a nucleotide sequence (SEQ ID NO:239) of a native sequence PRO6012 cDNA, wherein SEQ ID NO:239 is a clone designated herein as "DNA105794-2695".

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Figure 240 shows the amino acid sequence (SEQ ID NO:240) derived from the coding sequence of SEQ ID NO:239 shown in Figure 239.

Figure 241 shows a nucleotide sequence (SEQ ID NO:241) of a native sequence PRO6027 cDNA, wherein SEQ ID NO:241 is a clone designated herein as "DNA105838-2702".

Figure 242 shows the amino acid sequence (SEQ ID NO:242) derived from the coding sequence of SEQ ID NO:241 shown in Figure 241.

Figure 243 shows a nucleotide sequence (SEQ ID NO:243) of a native sequence PRO6181 cDNA, wherein SEQ ID NO:243 is a clone designated herein as "DNA107698-2715".

Figure 244 shows the amino acid sequence (SEQ ID NO:244) derived from the coding sequence of SEQ ID NO:243 shown in Figure 243.

Figure 245 shows a nucleotide sequence (SEQ ID NO:245) of a native sequence PRO6097 cDNA, wherein SEQ ID NO:245 is a clone designated herein as "DNA107701-2711".

Figure 246 shows the amino acid sequence (SEQ ID NO:246) derived from the coding sequence of SEQ ID NO:245 shown in Figure 245.

Figure 247 shows a nucleotide sequence (SEQ ID NO:247) of a native sequence PRO6090 cDNA, wherein SEQ ID NO:247 is a clone designated herein as "DNA107781-2707".

Figure 248 shows the amino acid sequence (SEQ ID NO:248) derived from the coding sequence of SEQ ID NO:247 shown in Figure 247.

Figure 249 shows a nucleotide sequence (SEQ ID NO:249) of a native sequence PRO7171 cDNA, wherein SEQ ID NO:249 is a clone designated herein as "DNA108670-2744".

Figure 250 shows the amino acid sequence (SEQ ID NO:250) derived from the coding sequence of SEQ ID NO:249 shown in Figure 249.

Figure 251 shows a nucleotide sequence (SEQ ID NO:251) of a native sequence PRO6258 cDNA, wherein SEQ ID NO:251 is a clone designated herein as "DNA108688-2725".

Figure 252 shows the amino acid sequence (SEQ ID NO:252) derived from the coding sequence of SEQ ID NO:251 shown in Figure 251.

Figure 253 shows a nucleotide sequence (SEQ ID NO:253) of a native sequence PRO9820 cDNA, wherein SEQ ID NO:253 is a clone designated herein as "DNA108769-2765".

Figure 254 shows the amino acid sequence (SEQ ID NO:254) derived from the coding sequence of SEQ ID NO:253 shown in Figure 253.

Figure 255 shows a nucleotide sequence (SEQ ID NO:255) of a native sequence PRO6243 cDNA, wherein SEQ ID NO:255 is a clone designated herein as "DNA108935-2721".

Figure 256 shows the amino acid sequence (SEQ ID NO:256) derived from the coding sequence of SEQ ID NO:255 shown in Figure 255.

Figure 257 shows a nucleotide sequence (SEQ ID NO:257) of a native sequence PRO6182 cDNA, wherein SEQ ID NO:257 is a clone designated herein as "DNA110700-2716".

Figure 258 shows the amino acid sequence (SEQ ID NO:258) derived from the coding sequence of SEQ ID NO:257 shown in Figure 257.

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Figure 259 shows a nucleotide sequence (SEQ ID NO:259) of a native sequence PRO6079 cDNA, wherein SEQ ID NO:259 is a clone designated herein as "DNA111750-2706".

Figure 260 shows the amino acid sequence (SEQ ID NO:260) derived from the coding sequence of SEQ ID NO:259 shown in Figure 259.

Figure 261 shows a nucleotide sequence (SEQ ID NO:261) of a native sequence PRO7434 cDNA, wherein SEQ ID NO:261 is a clone designated herein as "DNA123430-2755".

Figure 262 shows the amino acid sequence (SEQ ID NO:262) derived from the coding sequence of SEQ ID NO:261 shown in Figure 261.

Figure 263 shows a nucleotide sequence (SEQ ID NO:263) of a native sequence PRO9865 cDNA, wherein SEQ ID NO:263 is a clone designated herein as "DNA125154-2785".

Figure 264 shows the amino acid sequence (SEQ ID NO:264) derived from the coding sequence of SEQ ID NO:263 shown in Figure 263.

Figure 265 shows a nucleotide sequence (SEQ ID NO:265) of a native sequence PRO9828 cDNA, wherein SEQ ID NO:265 is a clone designated herein as "DNA142238-2768".

Figure 266 shows the amino acid sequence (SEQ ID NO:266) derived from the coding sequence of SEQ ID NO:265 shown in Figure 265.

Figure 267 shows a nucleotide sequence (SEQ ID NO:267) of a native sequence PRO196 cDNA, wherein SEQ ID NO:267 is a clone designated herein as "DNA22779-1130".

Figure 268 shows the amino acid sequence (SEQ ID NO:268) derived from the coding sequence of SEQ ID NO:267 shown in Figure 267.

Figure 269 shows a nucleotide sequence (SEQ ID NO:269) of a native sequence PRO197 cDNA, wherein SEQ ID NO:269 is a clone designated herein as "DNA22780-1078".

Figure 270 shows the amino acid sequence (SEQ ID NO:270) derived from the coding sequence of SEQ ID NO:269 shown in Figure 269.

Figure 271 shows a nucleotide sequence (SEQ ID NO:271) of a native sequence PRO195 cDNA, wherein SEQ ID NO:271 is a clone designated herein as "DNA26847-1395".

Figure 272 shows the amino acid sequence (SEQ ID NO:272) derived from the coding sequence of SEQ ID NO:271 shown in Figure 271.

Figure 273 shows a nucleotide sequence (SEQ ID NO:273) of a native sequence PRO187 cDNA, wherein SEQ ID NO:273 is a clone designated herein as "DNA27864-1155".

Figure 274 shows the amino acid sequence (SEQ ID NO:274) derived from the coding sequence of SEQ ID NO:273 shown in Figure 273.

Figure 275 shows a nucleotide sequence (SEQ ID NO:275) of a native sequence PRO182 cDNA, wherein SEQ ID NO:275 is a clone designated herein as "DNA27865-1091".

Figure 276 shows the amino acid sequence (SEQ ID NO:276) derived from the coding sequence of SEQ ID NO:275 shown in Figure 275.

Figure 277 shows a nucleotide sequence (SEQ ID NO:277) of a native sequence PRO188 cDNA, wherein SEQ ID NO:277 is a clone designated herein as "DNA28497-1130".

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Figure 278 shows the amino acid sequence (SEQ ID NO:278) derived from the coding sequence of SEQ ID NO:277 shown in Figure 277.

Figure 279 shows a nucleotide sequence (SEQ ID NO:279) of a native sequence PRO183 cDNA, wherein SEQ ID NO:279 is a clone designated herein as "DNA28498".

Figure 280 shows the amino acid sequence (SEQ ID NO:280) derived from the coding sequence of SEQ ID NO:279 shown in Figure 279.

Figure 281 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO184 cDNA, wherein SEQ ID NO:281 is a clone designated herein as "DNA28500".

Figure 282 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 281.

Figure 283 shows a nucleotide sequence (SEQ ID NO:283) of a native sequence PRO185 cDNA, wherein SEQ ID NO:283 is a clone designated herein as "DNA28503".

Figure 284 shows the amino acid sequence (SEQ ID NO:284) derived from the coding sequence of SEQ ID NO:283 shown in Figure 283.

Figure 285 shows a nucleotide sequence (SEQ ID NO:285) of a native sequence PRO200 cDNA, wherein SEQ ID NO:285 is a clone designated herein as "DNA29101-1122".

Figure 286 shows the amino acid sequence (SEQ ID NO:286) derived from the coding sequence of SEQ ID NO:285 shown in Figure 285.

Figure 287 shows a nucleotide sequence (SEQ ID NO:287) of a native sequence PRO202 cDNA, wherein SEQ ID NO:287 is a clone designated herein as "DNA30869".

Figure 288 shows the amino acid sequence (SEQ ID NO:288) derived from the coding sequence of SEQ ID NO:287 shown in Figure 287.

Figure 289 shows a nucleotide sequence (SEQ ID NO:289) of a native sequence PRO214 cDNA, wherein SEQ ID NO:289 is a clone designated herein as "DNA32286-1191".

Figure 290 shows the amino acid sequence (SEQ ID NO:290) derived from the coding sequence of SEQ ID NO:289 shown in Figure 289.

Figure 291 shows a nucleotide sequence (SEQ ID NO:291) of a native sequence PRO215 cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA32288-1132".

Figure 292 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ ID NO:291 shown in Figure 291.

Figure 293 shows a nucleotide sequence (SEQ ID NO:293) of a native sequence PRO219 cDNA, wherein SEQ ID NO:293 is a clone designated herein as "DNA32290-1164".

Figure 294 shows the amino acid sequence (SEQ ID NO:294) derived from the coding sequence of SEQ ID NO:293 shown in Figure 293.

Figure 295 shows a nucleotide sequence (SEQ ID NO:295) of a native sequence PRO211 cDNA, wherein SEQ ID NO:295 is a clone designated herein as "DNA32292-1131".

Figure 296 shows the amino acid sequence (SEQ ID NO:296) derived from the coding sequence of SEQ ID NO:295 shown in Figure 295.

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Figure 297 shows a nucleotide sequence (SEQ ID NO:297) of a native sequence PRO220 cDNA, wherein SEQ ID NO:297 is a clone designated herein as "DNA32298-1132".

Figure 298 shows the amino acid sequence (SEQ ID NO:298) derived from the coding sequence of SEQ ID NO:297 shown in Figure 297.

Figure 299 shows a nucleotide sequence (SEQ ID NO:299) of a native sequence PRO366 cDNA, wherein SEQ ID NO:299 is a clone designated herein as "DNA33085-1110".

Figure 300 shows the amino acid sequence (SEQ ID NO:300) derived from the coding sequence of SEQ ID NO:299 shown in Figure 299.

Figure 301 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO216 cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA33087-1158".

Figure 302 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 301.

Figure 303 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO221 cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA33089-1132".

Figure 304 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 303.

Figure 305 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO228 cDNA, wherein SEQ ID NO:305 is a clone designated herein as "DNA33092-1202".

Figure 306 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 305.

Figure 307 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO217 cDNA, wherein SEQ ID NO:307 is a clone designated herein as "DNA33094-1131".

Figure 308 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 307.

Figure 309 shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO222 cDNA, wherein SEQ ID NO:309 is a clone designated herein as "DNA33107-1135".

Figure 310 shows the amino acid sequence (SEQ ID NO:310) derived from the coding sequence of SEQ ID NO:309 shown in Figure 309.

Figure 311 shows a nucleotide sequence (SEQ ID NO:311) of a native sequence PRO224 cDNA, wherein SEQ ID NO:311 is a clone designated herein as "DNA33221-1133".

Figure 312 shows the amino acid sequence (SEQ ID NO:312) derived from the coding sequence of SEQ ID NO:311 shown in Figure 311.

Figure 313 shows a nucleotide sequence (SEQ ID NO:313) of a native sequence PRO230 cDNA, wherein SEQ ID NO:313 is a clone designated herein as "DNA33223-1136".

Figure 314 shows the amino acid sequence (SEQ ID NO:314) derived from the coding sequence of SEQ ID NO:313 shown in Figure 313.

Figure 315 shows a nucleotide sequence (SEQ ID NO:315) of a native sequence PRO198 cDNA, wherein SEQ ID NO:315 is a clone designated herein as "DNA33457-1078".

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Figure 316 shows the amino acid sequence (SEQ ID NO:316) derived from the coding sequence of SEQ ID NO:315 shown in Figure 315.

Figure 317 shows a nucleotide sequence (SEQ ID NO:317) of a native sequence PRO226 cDNA, wherein SEQ ID NO:317 is a clone designated herein as "DNA33460-1166".

Figure 318 shows the amino acid sequence (SEQ ID NO:318) derived from the coding sequence of SEQ ID NO:317 shown in Figure 317.

Figure 319 shows a nucleotide sequence (SEQ ID NO:319) of a native sequence PRO261 cDNA, wherein SEQ ID NO:319 is a clone designated herein as "DNA33473-1176".

Figure 320 shows the amino acid sequence (SEQ ID NO:320) derived from the coding sequence of SEQ ID NO:319 shown in Figure 319.

Figure 321 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO242 cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA33785-1143".

Figure 322 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 321.

Figure 323 shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO227 cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA33786-1132".

Figure 324 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 323.

Figure 325 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO237 cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA34353-1428".

Figure 326 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 325.

Figure 327 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO241 cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA34392-1170".

Figure 328 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 327.

Figure 329 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO231 cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA34434-1139".

Figure 330 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 329.

Figure 331 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence PRO235 cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA35558-1167".

Figure 332 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 331.

Figure 333 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO323 cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA35595-1228".

Figure 334 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 333.

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Figure 335 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO245 cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA35638-1216".

Figure 336 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of SEQ ID NO:335 shown in Figure 335.

Figure 337 shows a nucleotide sequence (SEQ ID NO:337) of a native sequence PRO246 cDNA, wherein SEQ ID NO:337 is a clone designated herein as "DNA35639-1172".

Figure 338 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 337.

Figure 339 shows a nucleotide sequence (SEQ ID NO:339) of a native sequence PRO288 cDNA, wherein SEQ ID NO:339 is a clone designated herein as "DNA35663-1129".

Figure 340 shows the amino acid sequence (SEQ ID NO:340) derived from the coding sequence of SEQ ID NO:339 shown in Figure 339.

Figure 341 shows a nucleotide sequence (SEQ ID NO:341) of a native sequence PRO248 cDNA, wherein SEQ ID NO:341 is a clone designated herein as "DNA35674-1142".

Figure 342 shows the amino acid sequence (SEQ ID NO:342) derived from the coding sequence of SEQ ID NO:341 shown in Figure 341.

Figure 343 shows a nucleotide sequence (SEQ ID NO:343) of a native sequence PRO257 cDNA, wherein SEQ ID NO:343 is a clone designated herein as "DNA35841-1173".

Figure 344 shows the amino acid sequence (SEQ ID NO:344) derived from the coding sequence of SEQ ID NO:343 shown in Figure 343.

Figure 345 shows a nucleotide sequence (SEQ ID NO:345) of a native sequence PRO172 cDNA, wherein SEQ ID NO:345 is a clone designated herein as "DNA35916-1161".

Figure 346 shows the amino acid sequence (SEQ ID NO:346) derived from the coding sequence of SEQ ID NO:345 shown in Figure 345.

Figure 347 shows a nucleotide sequence (SEQ ID NO:347) of a native sequence PRO258 cDNA, wherein SEQ ID NO:347 is a clone designated herein as "DNA35918-1174".

Figure 348 shows the amino acid sequence (SEQ ID NO:348) derived from the coding sequence of SEQ ID NO:347 shown in Figure 347.

Figure 349 shows a nucleotide sequence (SEQ ID NO:349) of a native sequence PRO265 cDNA, wherein SEQ ID NO:349 is a clone designated herein as "DNA36350-1158".

Figure 350 shows the amino acid sequence (SEQ ID NO:350) derived from the coding sequence of SEQ ID NO:349 shown in Figure 349.

Figure 351 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO326 cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA37140-1234".

Figure 352 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 351.

Figure 353 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO266 cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA37150-1178".

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Figure 354 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 353.

Figure 355 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO269 cDNA, wherein SEQ ID NO:355 is a clone designated herein as "DNA38260-1180".

Figure 356 shows the amino acid sequence (SEQ ID NO:356) derived from the coding sequence of SEQ ID NO:355 shown in Figure 355.

Figure 357 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO285 cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA40021-1154".

Figure 358 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 357.

Figure 359 shows a nucleotide sequence (SEQ ID NO:359) of a native sequence PRO328 cDNA, wherein SEQ ID NO:359 is a clone designated herein as "DNA40587-1231".

Figure 360 shows the amino acid sequence (SEQ ID NO:360) derived from the coding sequence of SEQ ID NO:359 shown in Figure 359.

Figure 361 shows a nucleotide sequence (SEQ ID NO:361) of a native sequence PRO344 cDNA, wherein SEQ ID NO:361 is a clone designated herein as "DNA40592-1242".

Figure 362 shows the amino acid sequence (SEQ ID NO:362) derived from the coding sequence of SEQ ID NO:361 shown in Figure 361.

Figure 363 shows a nucleotide sequence (SEQ ID NO:363) of a native sequence PRO272 cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA40620-1183".

Figure 364 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 363.

Figure 365 shows a nucleotide sequence (SEQ ID NO:365) of a native sequence PRO301 cDNA, wherein SEQ ID NO:365 is a clone designated herein as "DNA40628-1216".

Figure 366 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 365.

Figure 367 shows a nucleotide sequence (SEQ ID NO:367) of a native sequence PRO331 cDNA, wherein SEQ ID NO:367 is a clone designated herein as "DNA40981-1234".

Figure 368 shows the amino acid sequence (SEQ ID NO:368) derived from the coding sequence of SEQ ID NO:367 shown in Figure 367.

Figure 369 shows a nucleotide sequence (SEQ ID NO:369) of a native sequence PRO332 cDNA, wherein SEQ ID NO:369 is a clone designated herein as "DNA40982-1235".

Figure 370 shows the amino acid sequence (SEQ ID NO:370) derived from the coding sequence of SEQ ID NO:369 shown in Figure 369.

Figure 371 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO353 cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA41234-1242".

Figure 372 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 371.

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Figure 373 shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO310 cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA43046-1225".

Figure 374 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 373.

Figure 375 shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO337 cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA43316-1237".

Figure 376 shows the amino acid sequence (SEQ ID NO:376) derived from the coding sequence of SEQ ID NO:375 shown in Figure 375.

Figure 377 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO346 cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA44167-1243".

Figure 378 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 377.

Figure 379 shows a nucleotide sequence (SEQ ID NO:379) of a native sequence PRO350 cDNA, wherein SEQ ID NO:379 is a clone designated herein as "DNA44175-1314".

Figure 380 shows the amino acid sequence (SEQ ID NO:380) derived from the coding sequence of SEQ ID NO:379 shown in Figure 379.

Figure 381 shows a nucleotide sequence (SEQ ID NO:381) of a native sequence PRO526 cDNA, wherein SEQ ID NO:381 is a clone designated herein as "DNA44184-1319".

Figure 382 shows the amino acid sequence (SEQ ID NO:382) derived from the coding sequence of SEQ ID NO:381 shown in Figure 381.

Figure 383 shows a nucleotide sequence (SEQ ID NO:383) of a native sequence PRO381 cDNA, wherein SEQ ID NO:383 is a clone designated herein as "DNA44194-1317".

Figure 384 shows the amino acid sequence (SEQ ID NO:384) derived from the coding sequence of SEQ ID NO:383 shown in Figure 383.

Figure 385 shows a nucleotide sequence (SEQ ID NO:385) of a native sequence PRO846 cDNA, wherein SEQ ID NO:385 is a clone designated herein as "DNA44196-1353".

Figure 386 shows the amino acid sequence (SEQ ID NO:386) derived from the coding sequence of SEQ ID NO:385 shown in Figure 385.

Figure 387 shows a nucleotide sequence (SEQ ID NO:387) of a native sequence PRO363 cDNA, wherein SEQ ID NO:387 is a clone designated herein as "DNA45419-1252".

Figure 388 shows the amino acid sequence (SEQ ID NO:388) derived from the coding sequence of SEQ ID NO:387 shown in Figure 387.

Figure 389 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO365 cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA46777-1253".

Figure 390 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 389.

Figure 391 shows a nucleotide sequence (SEQ ID NO:391) of a native sequence PRO1310 cDNA, wherein SEQ ID NO:391 is a clone designated herein as "DNA47394-1572".

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Figure 392 shows the amino acid sequence (SEQ ID NO:392) derived from the coding sequence of SEQ ID NO:391 shown in Figure 391.

Figure 393 shows a nucleotide sequence (SEQ ID NO:393) of a native sequence PRO731 cDNA, wherein SEQ ID NO:393 is a clone designated herein as "DNA48331-1329".

Figure 394 shows the amino acid sequence (SEQ ID NO:394) derived from the coding sequence of SEQ ID NO:393 shown in Figure 393.

Figure 395 shows a nucleotide sequence (SEQ ID NO:395) of a native sequence PRO322 cDNA, wherein SEQ ID NO:395 is a clone designated herein as "DNA48336-1309".

Figure 396 shows the amino acid sequence (SEQ ID NO:396) derived from the coding sequence of SEQ ID NO:395 shown in Figure 395.

Figure 397 shows a nucleotide sequence (SEQ ID NO:397) of a native sequence PRO536 cDNA, wherein SEQ ID NO:397 is a clone designated herein as "DNA49142-1430".

Figure 398 shows the amino acid sequence (SEQ ID NO:398) derived from the coding sequence of SEQ ID NO:397 shown in Figure 397.

Figure 399 shows a nucleotide sequence (SEQ ID NO:399) of a native sequence PRO719 cDNA, wherein SEQ ID NO:399 is a clone designated herein as "DNA49646-1327".

Figure 400 shows the amino acid sequence (SEQ ID NO:400) derived from the coding sequence of SEQ ID NO:399 shown in Figure 399.

Figure 401 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO619 cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA49821-1562".

Figure 402 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 401.

Figure 403 shows a nucleotide sequence (SEQ ID NO:403) of a native sequence PRO771 cDNA, wherein SEQ ID NO:403 is a clone designated herein as "DNA49829-1346".

Figure 404 shows the amino acid sequence (SEQ ID NO:404) derived from the coding sequence of SEQ ID NO:403 shown in Figure 403.

Figure 405 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence PRO1083 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA50921-1458".

Figure 406 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 405.

Figure 407 shows a nucleotide sequence (SEQ ID NO:407) of a native sequence PRO862 cDNA, wherein SEQ ID NO:407 is a clone designated herein as "DNA52187-1354".

Figure 408 shows the amino acid sequence (SEQ ID NO:408) derived from the coding sequence of SEQ ID NO:407 shown in Figure 407.

Figure 409 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO733 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA52196-1348".

Figure 410 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 409.

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Figure 411 shows a nucleotide sequence (SEQ ID NO:411) of a native sequence PRO1188 cDNA, wherein SEQ ID NO:411 is a clone designated herein as "DNA52598-1518".

Figure 412 shows the amino acid sequence (SEQ ID NO:412) derived from the coding sequence of SEQ ID NO:411 shown in Figure 411.

Figure 413 shows a nucleotide sequence (SEQ ID NO:413) of a native sequence PRO770 cDNA, wherein SEQ ID NO:413 is a clone designated herein as "DNA54228-1366".

Figure 414 shows the amino acid sequence (SEQ ID NO:414) derived from the coding sequence of SEQ ID NO:413 shown in Figure 413.

Figure 415 shows a nucleotide sequence (SEQ ID NO:415) of a native sequence PRO1080 cDNA, wherein SEQ ID NO:415 is a clone designated herein as "DNA56047-1456".

Figure 416 shows the amino acid sequence (SEQ ID NO:416) derived from the coding sequence of SEQ ID NO:415 shown in Figure 415.

Figure 417 shows a nucleotide sequence (SEQ ID NO:417) of a native sequence PRO1017 cDNA, wherein SEQ ID NO:417 is a clone designated herein as "DNA56112-1379".

Figure 418 shows the amino acid sequence (SEQ ID NO:418) derived from the coding sequence of SEQ ID NO:417 shown in Figure 417.

Figure 419 shows a nucleotide sequence (SEQ ID NO:419) of a native sequence PRO1016 cDNA, wherein SEQ ID NO:419 is a clone designated herein as "DNA56113-1378".

Figure 420 shows the amino acid sequence (SEQ ID NO:420) derived from the coding sequence of SEQ ID NO:419 shown in Figure 419.

Figure 421 shows a nucleotide sequence (SEQ ID NO:421) of a native sequence PRO792 cDNA, wherein SEQ ID NO:421 is a clone designated herein as "DNA56352-1358".

Figure 422 shows the amino acid sequence (SEQ ID NO:422) derived from the coding sequence of SEQ ID NO:421 shown in Figure 421.

Figure 423 shows a nucleotide sequence (SEQ ID NO:423) of a native sequence PRO938 cDNA, wherein SEQ ID NO:423 is a clone designated herein as "DNA56433-1406".

Figure 424 shows the amino acid sequence (SEQ ID NO:424) derived from the coding sequence of SEQ ID NO:423 shown in Figure 423.

Figure 425 shows a nucleotide sequence (SEQ ID NO:425) of a native sequence PRO1012 cDNA, wherein SEQ ID NO:425 is a clone designated herein as "DNA56439-1376".

Figure 426 shows the amino acid sequence (SEQ ID NO:426) derived from the coding sequence of SEQ ID NO:425 shown in Figure 425.

Figure 427 shows a nucleotide sequence (SEQ ID NO:427) of a native sequence PRO1008 cDNA, wherein SEQ ID NO:427 is a clone designated herein as "DNA57530-1375".

Figure 428 shows the amino acid sequence (SEQ ID NO:428) derived from the coding sequence of SEQ ID NO:427 shown in Figure 427.

Figure 429 shows a nucleotide sequence (SEQ ID NO:429) of a native sequence PRO1075 cDNA, wherein SEQ ID NO:429 is a clone designated herein as "DNA57689-1385".

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Figure 430 shows the amino acid sequence (SEQ ID NO:430) derived from the coding sequence of SEQ ID NO:429 shown in Figure 429.

Figure 431 shows a nucleotide sequence (SEQ ID NO:431) of a native sequence PRO1007 cDNA, wherein SEQ ID NO:431 is a clone designated herein as "DNA57690-1374".

Figure 432 shows the amino acid sequence (SEQ ID NO:432) derived from the coding sequence of SEQ ID NO:431 shown in Figure 431.

Figure 433 shows a nucleotide sequence (SEQ ID NO:433) of a native sequence PRO1056 cDNA, wherein SEQ ID NO:433 is a clone designated herein as "DNA57693-1424".

Figure 434 shows the amino acid sequence (SEQ ID NO:434) derived from the coding sequence of SEQ ID NO:433 shown in Figure 433.

Figure 435 shows a nucleotide sequence (SEQ ID NO:435) of a native sequence PRO791 cDNA, wherein SEQ ID NO:435 is a clone designated herein as "DNA57838-1337".

Figure 436 shows the amino acid sequence (SEQ ID NO:436) derived from the coding sequence of SEQ ID NO:435 shown in Figure 435.

Figure 437 shows a nucleotide sequence (SEQ ID NO:437) of a native sequence PRO1111 cDNA, wherein SEQ ID NO:437 is a clone designated herein as "DNA58721-1475".

Figure 438 shows the amino acid sequence (SEQ ID NO:438) derived from the coding sequence of SEQ ID NO:437 shown in Figure 437.

Figure 439 shows a nucleotide sequence (SEQ ID NO:439) of a native sequence PRO812 cDNA, wherein SEQ ID NO:439 is a clone designated herein as "DNA59205-1421".

Figure 440 shows the amino acid sequence (SEQ ID NO:440) derived from the coding sequence of SEQ ID NO:439 shown in Figure 439.

Figure 441 shows a nucleotide sequence (SEQ ID NO:441) of a native sequence PRO1066 cDNA, wherein SEQ ID NO:441 is a clone designated herein as "DNA59215-1425".

Figure 442 shows the amino acid sequence (SEQ ID NO:442) derived from the coding sequence of SEQ ID NO:441 shown in Figure 441.

Figure 443 shows a nucleotide sequence (SEQ ID NO:443) of a native sequence PRO1185 cDNA, wherein SEQ ID NO:443 is a clone designated herein as "DNA59220-1514".

Figure 444 shows the amino acid sequence (SEQ ID NO:444) derived from the coding sequence of SEQ ID NO:443 shown in Figure 443.

Figure 445 shows a nucleotide sequence (SEQ ID NO:445) of a native sequence PRO1031 cDNA, wherein SEQ ID NO:445 is a clone designated herein as "DNA59294-1381".

Figure 446 shows the amino acid sequence (SEQ ID NO:446) derived from the coding sequence of SEQ ID NO:445 shown in Figure 445.

Figure 447 shows a nucleotide sequence (SEQ ID NO:447) of a native sequence PRO1360 cDNA, wherein SEQ ID NO:447 is a clone designated herein as "DNA59488-1603".

Figure 448 shows the amino acid sequence (SEQ ID NO:448) derived from the coding sequence of SEQ ID NO:447 shown in Figure 447.

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Figure 449 shows a nucleotide sequence (SEQ ID NO:449) of a native sequence PRO1309 cDNA, wherein SEQ ID NO:449 is a clone designated herein as "DNA59588-1571".

Figure 450 shows the amino acid sequence (SEQ ID NO:450) derived from the coding sequence of SEQ ID NO:449 shown in Figure 449.

Figure 451 shows a nucleotide sequence (SEQ ID NO:451) of a native sequence PRO1107 cDNA, wherein SEQ ID NO:451 is a clone designated herein as "DNA59606-1471".

Figure 452 shows the amino acid sequence (SEQ ID NO:452) derived from the coding sequence of SEQ ID NO:451 shown in Figure 451.

Figure 453 shows a nucleotide sequence (SEQ ID NO:453) of a native sequence PRO836 cDNA, wherein SEQ ID NO:453 is a clone designated herein as "DNA59620-1463".

Figure 454 shows the amino acid sequence (SEQ ID NO:454) derived from the coding sequence of SEQ ID NO:453 shown in Figure 453.

Figure 455 shows a nucleotide sequence (SEQ ID NO:455) of a native sequence PRO1132 cDNA, wherein SEQ ID NO:455 is a clone designated herein as "DNA59767-1489".

Figure 456 shows the amino acid sequence (SEQ ID NO:456) derived from the coding sequence of SEQ ID NO:455 shown in Figure 455.

Figure 457 shows a nucleotide sequence (SEQ ID NO:457) of a native sequence PRO1131 cDNA, wherein SEQ ID NO:457 is a clone designated herein as "DNA59777-1480".

Figure 458 shows the amino acid sequence (SEQ ID NO:458) derived from the coding sequence of SEQ ID NO:457 shown in Figure 457.

Figure 459 shows a nucleotide sequence (SEQ ID NO:459) of a native sequence PRO1130 cDNA, wherein SEQ ID NO:459 is a clone designated herein as "DNA59814-1486".

Figure 460 shows the amino acid sequence (SEQ ID NO:460) derived from the coding sequence of SEQ ID NO:459 shown in Figure 459.

Figure 461 shows a nucleotide sequence (SEQ ID NO:461) of a native sequence PRO844 cDNA, wherein SEQ ID NO:461 is a clone designated herein as "DNA59839-1461".

Figure 462 shows the amino acid sequence (SEQ ID NO:462) derived from the coding sequence of SEQ ID NO:461 shown in Figure 461.

Figure 463 shows a nucleotide sequence (SEQ ID NO:463) of a native sequence PRO1154 cDNA, wherein SEQ ID NO:463 is a clone designated herein as "DNA59846-1503".

Figure 464 shows the amino acid sequence (SEQ ID NO:464) derived from the coding sequence of SEQ ID NO:463 shown in Figure 463.

Figure 465 shows a nucleotide sequence (SEQ ID NO:465) of a native sequence PRO1181 cDNA, wherein SEQ ID NO:465 is a clone designated herein as "DNA59847-1511".

Figure 466 shows the amino acid sequence (SEQ ID NO:466) derived from the coding sequence of SEQ ID NO:465 shown in Figure 465.

Figure 467 shows a nucleotide sequence (SEQ ID NO:467) of a native sequence PRO1126 cDNA, wherein SEQ ID NO:467 is a clone designated herein as "DNA60615-1483".

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Figure 468 shows the amino acid sequence (SEQ ID NO:468) derived from the coding sequence of SEQ ID NO:467 shown in Figure 467.

Figure 469 shows a nucleotide sequence (SEQ ID NO:469) of a native sequence PRO1186 cDNA, wherein SEQ ID NO:469 is a clone designated herein as "DNA60621-1516".

Figure 470 shows the amino acid sequence (SEQ ID NO:470) derived from the coding sequence of SEQ ID NO:469 shown in Figure 469.

Figure 471 shows a nucleotide sequence (SEQ ID NO:471) of a native sequence PRO1198 cDNA, wherein SEQ ID NO:471 is a clone designated herein as "DNA60622-1525".

Figure 472 shows the amino acid sequence (SEQ ID NO:472) derived from the coding sequence of SEQ ID NO:471 shown in Figure 471.

Figure 473 shows a nucleotide sequence (SEQ ID NO:473) of a native sequence PRO1159 cDNA, wherein SEQ ID NO:473 is a clone designated herein as "DNA60627-1508".

Figure 474 shows the amino acid sequence (SEQ ID NO:474) derived from the coding sequence of SEQ ID NO:473 shown in Figure 473.

Figure 475 shows a nucleotide sequence (SEQ ID NO:475) of a native sequence PRO1265 cDNA, wherein SEQ ID NO:475 is a clone designated herein as "DNA60764-1533".

Figure 476 shows the amino acid sequence (SEQ ID NO:476) derived from the coding sequence of SEQ ID NO:475 shown in Figure 475.

Figure 477 shows a nucleotide sequence (SEQ ID NO:477) of a native sequence PRO1250 cDNA, wherein SEQ ID NO:477 is a clone designated herein as "DNA60775-1532".

Figure 478 shows the amino acid sequence (SEQ ID NO:478) derived from the coding sequence of SEQ ID NO:477 shown in Figure 477.

Figure 479 shows a nucleotide sequence (SEQ ID NO:479) of a native sequence PRO1475 cDNA, wherein SEQ ID NO:479 is a clone designated herein as "DNA61185-1646".

Figure 480 shows the amino acid sequence (SEQ ID NO:480) derived from the coding sequence of SEQ ID NO:479 shown in Figure 479.

Figure 481 shows a nucleotide sequence (SEQ ID NO:481) of a native sequence PRO1312 cDNA, wherein SEQ ID NO:481 is a clone designated herein as "DNA61873-1574".

Figure 482 shows the amino acid sequence (SEQ ID NO:482) derived from the coding sequence of SEQ ID NO:481 shown in Figure 481.

Figure 483 shows a nucleotide sequence (SEQ ID NO:483) of a native sequence PRO1308 cDNA, wherein SEQ ID NO:483 is a clone designated herein as "DNA62306-1570".

Figure 484 shows the amino acid sequence (SEQ ID NO:484) derived from the coding sequence of SEQ ID NO:483 shown in Figure 483.

Figure 485 shows a nucleotide sequence (SEQ ID NO:485) of a native sequence PRO1326 cDNA, wherein SEQ ID NO:485 is a clone designated herein as "DNA62808-1582".

Figure 486 shows the amino acid sequence (SEQ ID NO:486) derived from the coding sequence of SEQ ID NO:485 shown in Figure 485.

Figure 487 shows a nucleotide sequence (SEQ ID NO:487) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:487 is a clone designated herein as "DNA62814-1521".

Figure 488 shows the amino acid sequence (SEQ ID NO:488) derived from the coding sequence of SEQ ID NO:487 shown in Figure 487.

Figure 489 shows a nucleotide sequence (SEQ ID NO:489) of a native sequence PRO1246 cDNA, wherein SEQ ID NO:489 is a clone designated herein as "DNA64885-1529".

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Figure 490 shows the amino acid sequence (SEQ ID NO:490) derived from the coding sequence of SEQ ID NO:489 shown in Figure 489.

Figure 491 shows a nucleotide sequence (SEQ ID NO:491) of a native sequence PRO1356 cDNA, wherein SEQ ID NO:491 is a clone designated herein as "DNA64886-1601".

Figure 492 shows the amino acid sequence (SEQ ID NO:492) derived from the coding sequence of SEQ ID NO:491 shown in Figure 491.

Figure 493 shows a nucleotide sequence (SEQ ID NO:493) of a native sequence PRO1275 cDNA, wherein SEQ ID NO:493 is a clone designated herein as "DNA64888-1542".

Figure 494 shows the amino acid sequence (SEQ ID NO:494) derived from the coding sequence of SEQ ID NO:493 shown in Figure 493.

Figure 495 shows a nucleotide sequence (SEQ ID NO:495) of a native sequence PRO1274 cDNA, wherein SEQ ID NO:495 is a clone designated herein as "DNA64889-1541".

Figure 496 shows the amino acid sequence (SEQ ID NO:496) derived from the coding sequence of SEQ . ID NO:495 shown in Figure 495.

Figure 497 shows a nucleotide sequence (SEQ ID NO:497) of a native sequence PRO1358 cDNA, wherein SEQ ID NO:497 is a clone designated herein as "DNA64890-1612".

Figure 498 shows the amino acid sequence (SEQ ID NO:498) derived from the coding sequence of SEQ ID NO:497 shown in Figure 497.

Figure 499 shows a nucleotide sequence (SEQ ID NO:499) of a native sequence PRO1286 cDNA, wherein SEQ ID NO:499 is a clone designated herein as "DNA64903-1553".

Figure 500 shows the amino acid sequence (SEQ ID NO:500) derived from the coding sequence of SEQ ID NO:499 shown in Figure 499.

Figure 501 shows a nucleotide sequence (SEQ ID NO:501) of a native sequence PRO1294 cDNA, wherein SEQ ID NO:501 is a clone designated herein as "DNA64905-1558".

Figure 502 shows the amino acid sequence (SEQ ID NO:502) derived from the coding sequence of SEQ ID NO:501 shown in Figure 501.

Figure 503 shows a nucleotide sequence (SEQ ID NO:503) of a native sequence PRO1273 cDNA, wherein SEQ ID NO:503 is a clone designated herein as "DNA65402-1540".

Figure 504 shows the amino acid sequence (SEQ ID NO:504) derived from the coding sequence of SEQ ID NO:503 shown in Figure 503.

Figure 505 shows a nucleotide sequence (SEQ ID NO:505) of a native sequence PRO1279 cDNA, wherein SEQ ID NO:505 is a clone designated herein as "DNA65405-1547".

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Figure 506 shows the amino acid sequence (SEQ ID NO:506) derived from the coding sequence of SEQ ID NO:505 shown in Figure 505.

Figure 507 shows a nucleotide sequence (SEQ ID NO:507) of a native sequence PRO1195 cDNA, wherein SEQ ID NO:507 is a clone designated herein as "DNA65412-1523".

Figure 508 shows the amino acid sequence (SEQ ID NO:508) derived from the coding sequence of SEQ ID NO:507 shown in Figure 507.

Figure 509 shows a nucleotide sequence (SEQ ID NO:509) of a native sequence PRO1271 cDNA, wherein SEQ ID NO:509 is a clone designated herein as "DNA66309-1538".

Figure 510 shows the amino acid sequence (SEQ ID NO:510) derived from the coding sequence of SEQ ID NO:509 shown in Figure 509.

Figure 511 shows a nucleotide sequence (SEQ ID NO:511) of a native sequence PRO1338 cDNA, wherein SEQ ID NO:511 is a clone designated herein as "DNA66667-1596".

Figure 512 shows the amino acid sequence (SEQ ID NO:512) derived from the coding sequence of SEQ ID NO:511 shown in Figure 511.

Figure 513 shows a nucleotide sequence (SEQ ID NO:513) of a native sequence PRO1343 cDNA, wherein SEQ ID NO:513 is a clone designated herein as "DNA66675-1587".

Figure 514 shows the amino acid sequence (SEQ ID NO:514) derived from the coding sequence of SEQ ID NO:513 shown in Figure 513.

Figure 515 shows a nucleotide sequence (SEQ ID NO:515) of a native sequence PRO1434 cDNA, wherein SEQ ID NO:515 is a clone designated herein as "DNA68818-2536".

Figure 516 shows the amino acid sequence (SEQ ID NO:516) derived from the coding sequence of SEQ ID NO:515 shown in Figure 515.

Figure 517 shows a nucleotide sequence (SEQ ID NO:517) of a native sequence PRO1418 cDNA, wherein SEQ ID NO:517 is a clone designated herein as "DNA68864-1629".

Figure 518 shows the amino acid sequence (SEQ ID NO:518) derived from the coding sequence of SEQ ID NO:517 shown in Figure 517.

Figure 519 shows a nucleotide sequence (SEQ ID NO:519) of a native sequence PRO1387 cDNA, wherein SEQ ID NO:519 is a clone designated herein as "DNA68872-1620".

Figure 520 shows the amino acid sequence (SEQ ID NO:520) derived from the coding sequence of SEQ ID NO:519 shown in Figure 519.

Figure 521 shows a nucleotide sequence (SEQ ID NO:521) of a native sequence PRO1384 cDNA, wherein SEQ ID NO:521 is a clone designated herein as "DNA71159-1617".

Figure 522 shows the amino acid sequence (SEQ ID NO:522) derived from the coding sequence of SEQ ID NO:521 shown in Figure 521.

Figure 523 shows a nucleotide sequence (SEQ ID NO:523) of a native sequence PRO1565 cDNA, wherein SEQ ID NO:523 is a clone designated herein as "DNA73727-1673".

Figure 524 shows the amino acid sequence (SEQ ID NO:524) derived from the coding sequence of SEQ ID NO:523 shown in Figure 523.

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Figure 525 shows a nucleotide sequence (SEQ ID NO:525) of a native sequence PRO1474 cDNA, wherein SEQ ID NO:525 is a clone designated herein as "DNA73739-1645".

Figure 526 shows the amino acid sequence (SEQ ID NO:526) derived from the coding sequence of SEQ ID NO:525 shown in Figure 525.

Figure 527 shows a nucleotide sequence (SEQ ID NO:527) of a native sequence PRO1917 cDNA, wherein SEQ ID NO:527 is a clone designated herein as "DNA76400-2528".

Figure 528 shows the amino acid sequence (SEQ ID NO:528) derived from the coding sequence of SEQ ID NO:527 shown in Figure 527.

Figure 529 shows a nucleotide sequence (SEQ ID NO:529) of a native sequence PRO1787 cDNA, wherein SEQ ID NO:529 is a clone designated herein as "DNA76510-2504".

Figure 530 shows the amino acid sequence (SEQ ID NO:530) derived from the coding sequence of SEQ ID NO:529 shown in Figure 529.

Figure 531 shows a nucleotide sequence (SEQ ID NO:531) of a native sequence PRO1556 cDNA, wherein SEQ ID NO:531 is a clone designated herein as "DNA76529-1666".

Figure 532 shows the amino acid sequence (SEQ ID NO:532) derived from the coding sequence of SEQ ID NO:531 shown in Figure 531.

Figure 533 shows a nucleotide sequence (SEQ ID NO:533) of a native sequence PRO1561 cDNA, wherein SEQ ID NO:533 is a clone designated herein as "DNA76538-1670".

Figure 534 shows the amino acid sequence (SEQ ID NO:534) derived from the coding sequence of SEQ ID NO:533 shown in Figure 533.

Figure 535 shows a nucleotide sequence (SEQ ID NO:535) of a native sequence PRO1693 cDNA, wherein SEQ ID NO:535 is a clone designated herein as "DNA77301-1708".

Figure 536 shows the amino acid sequence (SEQ ID NO:536) derived from the coding sequence of SEQ ID NO:535 shown in Figure 535.

Figure 537 shows a nucleotide sequence (SEQ ID NO:537) of a native sequence PRO1868 cDNA, wherein SEQ ID NO:537 is a clone designated herein as "DNA77624-2515".

Figure 538 shows the amino acid sequence (SEQ ID NO:538) derived from the coding sequence of SEQ ID NO:537 shown in Figure 537.

Figure 539 shows a nucleotide sequence (SEQ ID NO:539) of a native sequence PRO1890 cDNA, wherein SEQ ID NO:539 is a clone designated herein as "DNA79230-2525".

Figure 540 shows the amino acid sequence (SEQ ID NO:540) derived from the coding sequence of SEQ ID NO:539 shown in Figure 539.

Figure 541 shows a nucleotide sequence (SEQ ID NO:541) of a native sequence PRO1887 cDNA, wherein SEQ ID NO:541 is a clone designated herein as "DNA79862-2522".

Figure 542 shows the amino acid sequence (SEQ ID NO:542) derived from the coding sequence of SEQ ID NO:541 shown in Figure 541.

Figure 543 shows a nucleotide sequence (SEQ ID NO:543) of a native sequence PRO4353 cDNA, wherein SEQ ID NO:543 is a clone designated herein as "DNA80145-2594".

Figure 544 shows the amino acid sequence (SEQ ID NO:544) derived from the coding sequence of SEQ ID NO:543 shown in Figure 543.

Figure 545 shows a nucleotide sequence (SEQ ID NO:545) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:545 is a clone designated herein as "DNA83500-2506".

Figure 546 shows the amino acid sequence (SEQ ID NO:546) derived from the coding sequence of SEQ ID NO:545 shown in Figure 545.

Figure 547 shows a nucleotide sequence (SEQ ID NO:547) of a native sequence PRO4357 cDNA, wherein SEQ ID NO:547 is a clone designated herein as "DNA84917-2597".

Figure 548 shows the amino acid sequence (SEQ ID NO:548) derived from the coding sequence of SEQ ID NO:547 shown in Figure 547.

Figure 549 shows a nucleotide sequence (SEQ ID NO:549) of a native sequence PRO4302 cDNA, wherein SEQ ID NO:549 is a clone designated herein as "DNA92218-2554".

Figure 550 shows the amino acid sequence (SEQ ID NO:550) derived from the coding sequence of SEQ ID NO:549 shown in Figure 549.

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

I. <u>Definitions</u>

The terms "PRO polypeptide" and "PRO" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and "PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. The term "PRO polypeptide" refers to each individual PRO/number polypeptide disclosed herein. All disclosures in this specification which refer to the "PRO polypeptide" refer to each of the polypeptides individually as well as jointly. For example, descriptions of the preparation of, purification of, derivation of, formation of antibodies to or against, administration of, compositions containing, treatment of a disease with, etc., pertain to each polypeptide of the invention individually. The term "PRO polypeptide" also includes variants of the PRO/number polypeptides disclosed herein.

A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be

isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the invention, the native sequence PRO polypeptides disclosed herein are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are comtemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the present specification and/or the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., Prot. Eng. 10:1-6 (1997) and von Heinje et al., Nucl. Acids. Res. 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present invention.

"PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for

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instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or Cterminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, alternatively at least about 20 amino acids in length, alternatively at least about 30 amino acids in length, alternatively at least about 40 amino acids in length, alternatively at least about 50 amino acids in length, alternatively at least about 60 amino acids in length, alternatively at least about 70 amino acids in length, alternatively at least about 80 amino acids in length, alternatively at least about 90 amino acids in length, alternatively at least about 100 amino acids in length, alternatively at least about 150 amino acids in length, alternatively at least about 200 amino acids in length, alternatively at least about 300 amino acids in length, or more.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly

available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

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where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Tables 2 and 3 demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated "Comparison Protein" to the amino acid sequence designated "PRO", wherein "PRO" represents the amino acid sequence of a hypothetical PRO polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, and "X, "Y" and "Z" each represent different hypothetical amino acid residues.

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Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % amino acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

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Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., <u>Nucleic Acids Res.</u> 25:3389-3402 (1997)). The NCBI-BLAST2 sequence

comparison program may be downloaded from http://www.ncbi.nlm.nih.gov or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

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where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

"PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity with a nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-

length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 210 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 270 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 900 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

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where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic

acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

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Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % nucleic acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When WU-BLAST-2 is employed, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptideencoding nucleic acid molecule of interest.

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., <u>Nucleic Acids Res.</u> 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from http://www.ncbi.nlm.nih.gov or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to

C.

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In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide in situ within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" PRO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the specific polypeptide-encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

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"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50° C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42° C; or (3) employ 50% formamide, $5 \times SSC$ (0.75 M NaCl, 0.075 M sodium citrate), $50 \times SSC$ (0.75 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, $5 \times SSC$ (0.75 mM sodium, sonicated salmon sperm DNA ($50 \times SSC$), $0.1\% \times SSC$, and $0.1\% \times SSC$ (sodium chloride/sodium citrate) and $0.1\% \times SSC$ (sodium chloride/sodium citrate) and $0.1\% \times SSC$ (solium chloride/sodium citrate) and 0.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent that those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO polypeptide fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not

substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

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"Active" or "activity" for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an "immunological" activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.

The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

"Treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEENTM, polyethylene glycol (PEG), and PLURONICSTM.

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"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv fragments; diabodies; linear antibodies (Zapata et al., <u>Protein Eng.</u> 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an F(ab')₂ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigenbinding site on the surface of the $V_{H^-}V_L$ dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')₂ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and

IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

"Single-chain Fv" or "sFv" antibody fragments comprise the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in <u>The Pharmacology of Monoclonal Antibodies</u>, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

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The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) in the same polypeptide chain (V_H-V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

An antibody that "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide is one that binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The

components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

An "effective amount" of a polypeptide disclosed herein or an agonist or antagonist thereof is an amount sufficient to carry out a specifically stated purpose. An "effective amount" may be determined empirically and in a routine manner, in relation to the stated purpose.

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Table 1

```
/*
         * C-C increased from 12 to 15
         * Z is average of EO
  5
         * B is average of ND
         * match with stop is M; stop-stop = 0; J (joker) match = 0
         */
        #define M
                                 /* value of a match with a stop */
10
                  day[26][26] = {
        /*
                A B C D E F G H I J K L M N O P Q R S T U V W X Y Z */
        /* A */
                   { 2, 0,-2, 0, 0,-4, 1,-1,-1, 0,-1,-2,-1, 0, M, 1, 0,-2, 1, 1, 0, 0,-6, 0,-3, 0},
        /* B */
                   \{0, 3, -4, 3, 2, -5, 0, 1, -2, 0, 0, -3, -2, 2, M, -1, 1, 0, 0, 0, 0, -2, -5, 0, -3, 1\},\
        /* C */
                   {-2,-4,15,-5,-5,-4,-3,-3,-2, 0,-5,-6,-5,-4, M,-3,-5,-4, 0,-2, 0,-2,-8, 0, 0,-5},
15
        /* D */
                   \{0, 3, -5, 4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 2\},\
        /* E */
                   { 0, 2,-5, 3, 4,-5, 0, 1,-2, 0, 0,-3,-2, 1, M,-1, 2,-1, 0, 0, 0,-2,-7, 0,-4, 3},
        /* F */
                   \{-4,-5,-4,-6,-5,9,-5,-2,1,0,-5,2,0,-4,\_M,-5,-5,-4,-3,-3,0,-1,0,0,7,-5\},
        /* G */
                   \{1, 0, -3, 1, 0, -5, 5, -2, -3, 0, -2, -4, -3, 0, M, -1, -1, -3, 1, 0, 0, -1, -7, 0, -5, 0\},\
                   /* H */
20
        /* I */
        /* ] */
        /* K */
                   {-1, 0,-5, 0, 0,-5,-2, 0,-2, 0, 5,-3, 0, 1, M,-1, 1, 3, 0, 0, 0,-2,-3, 0,-4, 0},
        /* L */
                   {-2,-3,-6,-4,-3, 2,-4,-2, 2, 0,-3, 6, 4,-3, M,-3,-2,-3,-3,-1, 0, 2,-2, 0,-1,-2},
        /* M */
                   \{-1,-2,-5,-3,-2,0,-3,-2,2,0,0,4,6,-2,M,-2,-1,0,-2,-1,0,2,-4,0,-2,-1\},
25
        /* N */
                   { 0, 2, -4, 2, 1, -4, 0, 2, -2, 0, 1, -3, -2, 2, M, -1, 1, 0, 1, 0, 0, -2, -4, 0, -2, 1},
        /* O */
                  /* P */
                   \{1,-1,-3,-1,-1,-5,-1,0,-2,0,-1,-3,-2,-1,M,6,0,0,1,0,0,-1,-6,0,-5,0\},
        /* Q */
                   { 0, 1,-5, 2, 2,-5,-1, 3,-2, 0, 1,-2,-1, 1, M, 0, 4, 1,-1,-1, 0,-2,-5, 0,-4, 3}, {-2, 0,-4,-1,-1,-4,-3, 2,-2, 0, 3,-3, 0, 0, M, 0, 1, 6, 0,-1, 0,-2, 2, 0,-4, 0},
        /* R */
30
        /* S */
                   \{1, 0, 0, 0, 0, -3, 1, -1, -1, 0, 0, -3, -2, 1, M, 1, -1, 0, 2, 1, 0, -1, -2, 0, -3, 0\},\
        /* T */
                   { 1, 0,-2, 0, 0,-3, 0,-1, 0, 0, 0,-1,-1, 0, M, 0,-1,-1, 1, 3, 0, 0,-5, 0,-3, 0},
        /* U */
                   /* V */
                   { 0,-2,-2,-2,-1,-1,-2, 4, 0,-2, 2, 2,-2,_M,-1,-2,-2,-1, 0, 0, 4,-6, 0,-2,-2},
        /* W */
                   {-6,-5,-8,-7,-7, 0,-7,-3,-5, 0,-3,-2,-4,-4, M,-6,-5, 2,-2,-5, 0,-6,17, 0, 0,-6},
35
        /* X */
                   /* Y */
                   {-3,-3, 0,-4,-4, 7,-5, 0,-1, 0,-4,-1,-2,-2, M,-5,-4,-4,-3,-3, 0,-2, 0, 0,10,-4},
        /* Z */
                  { 0, 1,-5, 2, 3,-5, 0, 2,-2, 0, 0,-2,-1, 1, M, 0, 3, 0, 0, 0, 0, -2,-6, 0,-4, 4}
        };
40
```

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```
/*
          */
         #include < stdio.h >
         #include < ctype.h >
  5
         #define MAXJMP
                                     16
                                               /* max jumps in a diag */
         #define MAXGAP
                                     24
                                               /* don't continue to penalize gaps larger than this */
         #define JMPS
                                     1024
                                               /* max jmps in an path */
         #define MX
                                               /* save if there's at least MX-1 bases since last jmp */
                                     4
 10
         #define DMAT
                                     3
                                               /* value of matching bases */
         #define DMIS
                                     0
                                               /* penalty for mismatched bases */
         #define DINS0
                                               /* penalty for a gap */
                                     8
         #define DINS1
                                     1
                                               /* penalty per base */
 15
         #define PINS0
                                               /* penalty for a gap */
         #define PINS1
                                               /* penalty per residue */
         struct jmp {
                                     n[MAXJMP];
                                                        /* size of jmp (neg for dely) */
20
                  unsigned short
                                     x[MAXJMP];
                                                        /* base no. of jmp in seq x */
         };
                                                        /* limits seq to 2^16 -1 */
         struct diag {
                                                        /* score at last jmp */
                  int
                                     score;
25
                  long
                                                        /* offset of prev block */
                                     offset;
                  short
                                                        /* current imp index */
                                     ijmp;
                  struct imp
                                     ip;
                                                        /* list of imps */
         };
30
         struct path {
                                               /* number of leading spaces */
                           n[JMPS];/* size of jmp (gap) */
                  short
                           x[JMPS];/* loc of jmp (last elem before gap) */
         };
35
                            *ofile;
         char
                                                        /* output file name */
         char
                            *namex[2];
                                                        /* seq names: getseqs() */
         char
                            *prog;
                                                        /* prog name for err msgs */
         char
                            *seqx[2];
                                                        /* seqs: getseqs() */
40
                           dmax;
                                                        /* best diag: nw() */
         int
                           dmax0;
         int
                                                        /* final diag */
         int
                           dna;
                                                        /* set if dna: main() */
                                                        /* set if penalizing end gaps */
         int
                           endgaps;
         int
                                                        /* total gaps in seqs */
                           gapx, gapy;
45
                                                        /* seq lens */
         int
                           len0, len1;
         int
                           ngapx, ngapy;
                                                        /* total size of gaps */
         int
                           smax;
                                                        /* max score: nw() */
         int
                           *xbm;
                                                        /* bitmap for matching */
         long
                           offset;
                                                        /* current offset in jmp file */
50
         struct
                  diag
                           *dx;
                                                        /* holds diagonals */
                                                        /* holds path for seqs */
         struct
                  path
                           pp[2];
         char
                           *calloc(), *malloc(), *index(), *strcpy();
         char
                           *getseq(), *g_calloc();
55
```

```
/* Needleman-Wunsch alignment program
          * usage: progs file1 file2
            where file1 and file2 are two dna or two protein sequences.
 5
             The sequences can be in upper- or lower-case an may contain ambiguity
             Any lines beginning with ';', '>' or '<' are ignored
             Max file length is 65535 (limited by unsigned short x in the jmp struct)
             A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
             Output is in the file "align.out"
10
          * The program may create a tmp file in /tmp to hold info about traceback.
          * Original version developed under BSD 4.3 on a vax 8650
         #include "nw.h"
15
         #include "day.h"
         static
                   dbval[26] = {
                  1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
         };
20
         static
                   _{pbval{26}} = {
                  \overline{1}, 2|(1 < <('D'-'A'))|(1 < <('N'-'A')), 4, 8, 16, 32, 64,
                  128, 256, 0xFFFFFFF, 1 < < 10, 1 < < 11, 1 < < 12, 1 < < 13, 1 < < 14,
                  1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
25
                  1 < <23, 1 < <24, 1 < <25 | (1 < <('E'-'A')) | (1 < <('Q'-'A'))
        };
                                                                                                                          main
        main(ac, av)
                  int
                            ac:
30
                  char
                            *av[];
        {
                  prog = av[0];
                  if (ac != 3)  {
                            fprintf(stderr, "usage: %s file1 file2\n", prog);
35
                            fprintf(stderr, "where file1 and file2 are two dna or two protein sequences.\n");
                            fprintf(stderr, "The sequences can be in upper- or lower-case\n");
                            fprintf(stderr, "Any lines beginning with ';' or '<' are ignored\n");
                           fprintf(stderr, "Output is in the file \"align.out\"\n");
                           exit(1);
40
                  namex[0] = av[1];
                  namex[1] = av[2];
                  seqx[0] = getseq(namex[0], \&len0);
                  seqx[1] = getseq(namex[1], &len1);
45
                  xbm = (dna)? _dbval : _pbval;
                  endgaps = 0;
                                                        /* 1 to penalize endgaps */
                  ofile = "align.out";
                                                        /* output file */
50
                                    /* fill in the matrix, get the possible jmps */
                  readjmps();
                                    /* get the actual jmps */
                  print();
                                    /* print stats, alignment */
                  cleanup(0);
                                    /* unlink any tmp files */
55
        }
```

Table 1 (cont')

```
/* do the alignment, return best score: main()
          * dna: values in Fitch and Smith, PNAS, 80, 1382-1386, 1983
          * pro: PAM 250 values
          * When scores are equal, we prefer mismatches to any gap, prefer
  5
          * a new gap to extending an ongoing gap, and prefer a gap in seqx
          * to a gap in seq y.
                                                                                                                             nw
         nw()
         {
10
                                      *px, *py;
                                                                  /* seqs and ptrs */
                                                         /* keep track of dely */
                                      *ndely, *dely;
                   int
                   int
                                                        /* keep track of delx */
                                     ndelx, delx;
                   int
                                      *tmp;
                                                        /* for swapping row0, row1 */
                   int
                                     mis;
                                                        /* score for each type */
15
                                                        /* insertion penalties */
                   int
                                     ins0, ins1;
                                                        /* diagonal index */
                  register
                                     id;
                   register
                                                        /* jmp index */
                                     ij;
                   register
                                      *col0, *col1;
                                                        /* score for curr, last row */
                                                        /* index into seqs */
                   register
                                     xx, yy;
20
                   dx = (struct diag *)g_calloc("to get diags", len0+len1+1, sizeof(struct diag));
                  ndely = (int *)g_calloc("to get ndely", len1+1, sizeof(int));
                  dely = (int *)g_calloc("to get dely", len1 + 1, sizeof(int));
25
                  col0 = (int *)g_calloc("to get col0", len1 + 1, sizeof(int));
                  col1 = (int *)g_calloc("to get col1", len1+1, sizeof(int));
                  ins0 = (dna)? DINS0 : PINS0;
                  ins1 = (dna)? DINS1: PINS1;
30
                  smax = -10000;
                  if (endgaps) {
                            for (col0[0] = dely[0] = -ins0, yy = 1; yy < = len1; yy + +) {
                                     col0[yy] = dely[yy] = col0[yy-1] - ins1;
                                     ndely[yy] = yy;
35
                           col0[0] = 0;
                                               /* Waterman Bull Math Biol 84 */
                  }
                  else
                           for (yy = 1; yy < = len1; yy++)
40
                                     dely[yy] = -ins0;
                  /* fill in match matrix
                   */
                  for (px = seqx[0], xx = 1; xx <= len0; px++, xx++) {
45
                           /* initialize first entry in col
                           if (endgaps) {
                                     if (xx == 1)
                                              col1[0] = delx = -(ins0+ins1);
50
                                              col1[0] = delx = col0[0] - ins1;
                                     ndelx = xx;
                           }
                           else {
55
                                     col1[0] = 0;
                                     delx = -ins0;
                                     ndelx = 0;
                           }
```

60

Table 1 (cont')

```
...nw
                          for (py = seqx[1], yy = 1; yy < = len1; py++, yy++) {
                                   mis = col0[yy-1];
                                   if (dna)
 5
                                            mis += (xbm[*px-'A']&xbm[*py-'A'])? DMAT : DMIS;
                                   else
                                            mis += _day[*px-'A'][*py-'A'];
                                   /* update penalty for del in x seq;
10
                                   * favor new del over ongong del
                                   * ignore MAXGAP if weighting endgaps
                                   if (endgaps | | ndely[yy] < MAXGAP) {
                                            if (col0[yy] - ins0 > = dely[yy]) {
15
                                                     dely[yy] = col0[yy] - (ins0 + ins1);
                                                     ndely[yy] = 1;
                                            } else {
                                                     dely[yy] -= ins1;
                                                     ndely[yy] + +;
20
                                            }
                                   } else {
                                            if (col0[yy] - (ins0 + ins1) > = dely[yy]) {
                                                     dely[yy] = col0[yy] - (ins0+ins1);
                                                     ndely[yy] = 1;
25
                                            } else
                                                     ndely[yy]++;
                                   }
                                   /* update penalty for del in y seq;
30
                                    * favor new del over ongong del
                                   if (endgaps | | ndelx < MAXGAP) {
                                            if (coll[yy-1] - ins0 > = delx) {
                                                     delx = col1[yy-1] - (ins0+ins1);
35
                                                     ndelx = 1;
                                            } else {
                                                     delx -= ins1;
                                                     ndelx + +;
                                            }
40
                                   } else {
                                            if (col1[yy-1] - (ins0 + ins1) > = delx) {
                                                     delx = coll[yy-1] - (ins0+ins1);
                                                     ndelx = 1;
                                            } else
45
                                                     ndelx++;
                                   }
                                   /* pick the maximum score; we're favoring
                                    * mis over any del and delx over dely
50
55
```

60

```
...nw
                                    id = xx - yy + lenl - 1;
                                    if (mis > = delx && mis > = dely[yy])
                                             coll[yy] = mis;
 5
                                    else if (delx > = dely[yy]) {
                                             coll[yy] = delx;
                                             ij = dx[id].ijmp;
                                             if (dx[id].jp.n[0] && (!dna | | (ndelx > = MAXJMP))
                                             && xx > dx[id].jp.x[ij]+MX) \mid \mid mis > dx[id].score+DINS0)) {
10
                                                      dx[id].ijmp++;
                                                      if (++ij > = MAXJMP) {
                                                                writejmps(id);
                                                                ij = dx[id].iimp = 0;
                                                                dx[id].offset = offset;
15
                                                                offset += sizeof(struct jmp) + sizeof(offset);
                                                      }
                                             dx[id].jp.n[ij] = ndelx;
                                             dx[id].jp.x[ij] = xx;
20
                                             dx[id].score = delx;
                                    else {
                                             coll[yy] = dely[yy];
                                             ij = dx[id].ijmp;
25
                 if (dx[id].jp.n[0] && (!dna | | (ndely[yy] > = MAXJMP)
                                             && xx > dx[id].jp.x[ij]+MX) \mid \mid mis > dx[id].score+DINS0)) {
                                                      dx[id].ijmp++;
                                                      if(++ij > = MAXJMP) 
                                                                writejmps(id);
30
                                                                ij = dx[id].ijmp = 0;
                                                                dx[id].offset = offset;
                                                                offset += sizeof(struct jmp) + sizeof(offset);
                                                      }
35
                                             dx[id].jp.n[ij] = -ndely[yy];
                                             dx[id].jp.x[ij] = xx;
                                             dx[id].score = dely[yy];
                                    } if (xx == len0 && yy < len1) {
40
                                             /* last col
                                             if (endgaps)
                                                      coll[yy] = ins0 + ins1*(len1-yy);
                                             if (coll[yy] > smax) {
45
                                                      smax = coll[yy];
                                                      dmax = id;
                                             }
                                    }
50
                          if (endgaps && xx < len0)
                                    coll{yy-1} -= ins0 + ins1*(len0-xx);
                          if (coll[yy-1] > smax) {
                                    smax = col1[yy-1];
                                    dmax = id;
55
                          tmp = col0; col0 = col1; col1 = tmp;
                 (void) free((char *)ndely);
                 (void) free((char *)dely);
60
                 (void) free((char *)col0);
                 (void) free((char *)col1);
                                                                }
```

Table 1 (cont')

```
* print() -- only routine visible outside this module
 5
          * getmat() -- trace back best path, count matches: print()
          * pr_align() -- print alignment of described in array p[]: print()
          * dumpblock() -- dump a block of lines with numbers, stars: pr_align()
          * nums() -- put out a number line: dumpblock()
10
          * putline() -- put out a line (name, [num], seq, [num]): dumpblock()
          * stars() - -put a line of stars: dumpblock()
          * stripname() -- strip any path and prefix from a seqname
15
        #include "nw.h"
         #define SPC
         #define P_LINE 256
                                       /* maximum output line */
         #define P_SPC
                                       /* space between name or num and seq */
                            3
20
         extern
                   _day[26][26];
                                       /* set output line length */
                   olen;
         int
                                       /* output file */
         FILE
                   *fx;
                                                                                                                                print
25
         print()
         {
                                                          /* overlap */
                   int
                             lx, ly, firstgap, lastgap;
                   if ((fx = fopen(ofile, "w")) == 0) {
30
                             fprintf(stderr, "%s: can't write %s\n", prog, ofile);
                             cleanup(1);
                  fprintf(fx, "< first sequence: %s (length = %d)\n", namex[0], lcn0); fprintf(fx, "< second sequence: %s (length = %d)\n", namex[1], len1);
35
                   olen = 60;
                  lx = len0;
                  ly = len1;
                   firstgap = lastgap = 0;
                   if (dmax < len1 - 1) {
                                                 /* leading gap in x */
40
                            pp[0].spc = firstgap = len1 - dmax - 1;
                             ly -= pp[0].spc;
                   else if (dmax > len1 - 1) { /* leading gap in y */
                            pp[1].spc = firstgap = dmax - (len1 - 1);
45
                             lx -= pp[1].spc;
                   if (dmax0 < len0 - 1) 
                                                 /* trailing gap in x */
                            lastgap = len0 - dmax0 - 1;
                            lx -= lastgap;
50
                  else if (dmax0 > len0 - 1) { /* trailing gap in y */
                            lastgap = dmax0 - (len0 - 1);
                             ly -= lastgap;
55
                   getmat(lx, ly, firstgap, lastgap);
                  pr_align();
         }
```

60

```
* trace back the best path, count matches
         */
        static
 5
        getmat(lx, ly, firstgap, lastgap)
                                                                                                                    getmat
                 int
                           lx, ly;
                                                       /* "core" (minus endgaps) */
                 int
                           firstgap, lastgap;
                                                       /* leading trailing overlap */
        {
                 int
                                    nm, i0, i1, siz0, siz1;
10
                  char
                                    outx[32];
                  double
                                    pct;
                  register
                                    n0, n1;
                 register char
                                    *p0, *p1;
15
                 /* get total matches, score
                  i0 = i1 = siz0 = siz1 = 0;
                 p0 = seqx[0] + pp[1].spc;
                 p1 = seqx[1] + pp[0].spc;
20
                 n0 = pp[1].spc + 1;
                 n1 = pp[0].spc + 1;
                 nm = 0;
                  while ( *p0 && *p1 ) {
25
                           if (siz0) {
                                    p1 + +;
                                    n1++;
                                    siz0--;
                           }
30
                          else if (siz1) {
                                    p0++:
                                    n0++;
                                    siz1--;
35
                          else {
                                    if (xbm[*p0-'A']&xbm[*p1-'A'])
                                             nm++;
                                    if (n0++==pp[0].x[i0])
                                             siz0 = pp[0].n[i0++];
40
                                    if (n1 + + = = pp[1].x[i1])
                                             siz1 = pp[1].n[i1++];
                                    p0++;
                                    p1 + +;
                          }
45
                 }
                 /* pct homology:
                  * if penalizing endgaps, base is the shorter seq
                  * else, knock off overhangs and take shorter core
50
                  */
                 if (endgaps)
                          lx = (len0 < len1)? len0 : len1;
                          lx = (lx < ly)? lx : ly;
55
                 pct = 100.*(double)nm/(double)lx;
                 fprintf(fx, "\n");
                 fprintf(fx, "< %d match%s in an overlap of %d: %.2f percent similarity\n",
                          nm, (nm = = 1)? "" : "es", lx, pct);
60
```

```
...getmat
                   fprintf(fx, " < gaps in first sequence: %d", gapx);
                   if (gapx) {
                            (void) sprintf(outx, " (%d %s%s)",
  5
                                     ngapx, (dna)? "base": "residue", (ngapx = = 1)? "": "s");
                            fprintf(fx, "%s", outx);
                   fprintf(fx, ", gaps in second sequence: %d", gapy);
                   if (gapy) {
 10
                            (void) sprintf(outx, " (%d %s%s)",
                                     ngapy, (dna)? "base": "residue", (ngapy == 1)? "": "s");
                            fprintf(fx, "%s", outx);
                   if (dna)
15
                            fprintf(fx,
                            "\n < score: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)\n",
                            smax, DMAT, DMIS, DINSO, DINS1);
                   else
20
                            "\n < score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n",
                            smax, PINSO, PINS1);
                  if (endgaps)
                            fprintf(fx,
                            "<endgaps penalized. left endgap: %d %s%s, right endgap: %d %s%s\n",
25
                            firstgap, (dna)? "base": "residue", (firstgap = = 1)? "": "s",
                            lastgap, (dna)? "base" : "residue", (lastgap == 1)? "" : "s");
                  else
                            fprintf(fx, "<endgaps not penalized\n");</pre>
         }
30
         static
                            nm;
                                               /* matches in core -- for checking */
         static
                            lmax;
                                               /* lengths of stripped file names */
         static
                            ij[2];
                                               /* jmp index for a path */
         static
                            nc[2];
                                               /* number at start of current line */
35
         static
                                              /* current elem number -- for gapping */
                            ni[2];
         static
                            siz[2];
         static char
                            *ps[2];
                                               /* ptr to current element */
         static char
                            *po[2];
                                              /* ptr to next output char slot */
                            out[2][P_LINE];
         static char
                                             /* output line */
40
         static char
                            star[P LINE];
                                               /* set by stars() */
         * print alignment of described in struct path pp[]
45
        static
                                                                                                                     pr align
        pr_align()
         {
                  int
                                     nn;
                                              /* char count */
                  int
                                     тоге;
50
                  register
                                    i;
                  for (i = 0, lmax = 0; i < 2; i++) {
                           nn = stripname(namex[i]);
                           if (nn > lmax)
55
                                    lmax = nn;
                           nc[i] = 1;
                           ni[i] = 1;
                           siz[i] = ij[i] = 0;
60
                           ps[i] = seqx[i];
                           po[i] = out[i];
                                                                 }
```

```
...pr_align
                 for (nn = nm = 0, more = 1; more;)
                           for (i = more = 0; i < 2; i++)
 5
                                    * do we have more of this sequence?
                                    */
                                    if (!*ps[i])
                                             continue;
10
                                    more++;
                                    if (pp[i].spc) { /* leading space */
                                             *po[i]++ = ' ';
                                             pp[i].spc--;
15
                                    else if (siz[i]) { /* in a gap */
                                              *po[i] + + = '-';
                                              siz[i]--;
                                    }
20
                                    else {
                                                       /* we're putting a seq element
                                              *po[i] = *ps[i];
                                             if (islower(*ps[i]))
                                                      *ps[i] = toupper(*ps[i]);
25
                                             ps[i]++;
                                              * are we at next gap for this seq?
30.
                                               if (ni[i] == pp[i].x[ij[i]]) \{
                                                        * we need to merge all gaps
                                                        * at this location
35
                                                       siz[i] = pp[i].n[ij[i]++];
                                                       while (ni[i] == pp[i].x[ij[i]])

siz[i] += pp[i].n[ij[i]++];
40
                                              ni[i]++;
                                    }
                           if (++nn = = olen | | !more && nn) {
                                    dumpblock();
45
                                    for (i = 0; i < 2; i++)
                                             po[i] = out[i];
                                    nn = 0;
                           }
                 }
50
        }
         * dump a block of lines, including numbers, stars: pr_align()
55
        static
                                                                                                               dumpblock
        dumpblock()
        {
                  register i;
60
                  for (i = 0; i < 2; i++)
                           *po[i] - = '0';
```

```
...dumpblock
                  (void) putc('\n', fx);
                 for (i = 0; i < 2; i++) {
 5
                           if (*out[i] && (*out[i] != ' ' | | *(po[i]) != ' ')) {
                                    if (i == 0)
                                              nums(i);
                                    if (i == 0 \&\& *out[1])
                                              stars();
10
                                    putline(i);
                                    if (i == 0 && *out[1])
                                              fprintf(fx, star);
                                    if (i == 1)
                                              nums(i);
15
                           }
                 }
        }
20
         * put out a number line: dumpblock()
        static
        nums(ix)
                                                                                                                       nums
                                    /* index in out[] holding seq line */
                 int
                           ix;
25
        {
                  char
                                    nline[P LINE];
                  register
                                    i, j;
                 register char
                                    *pn, *px, *py;
30
                 for (pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
                           *pn = ' ';
                 for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
                           if (*py == ' ' | | *py == '-')
*pn = ' ';
35
                           else {
                                    if (i\%10 == 0 | | (i == 1 \&\& nc[ix] != 1)) {
                                             j = (i < 0)? -i : i;
                                              for (px = pn; j; j /= 10, px--)
                                                       *px = j\%10 + '0';
40
                                              if (i < 0)
                                                       px = '-';
                                    }
                                    else
                                              *pn = ' ';
45
                                    i++;
                           }
                  *pn = '\0';
                 nc[ix] = i;
50
                 for (pn = nline; *pn; pn++)
                           (void) putc(*pn, fx);
                 (void) putc('\n', fx);
        }
55
         * put out a line (name, [num], seq, [num]): dumpblock()
        static
                                                                                                                    putline
        putline(ix)
60
                 int
                                                       {
                           ix;
```

Table 1 (cont')

```
...putline
                 int
                                    i;
                 register char
                                    *px;
 5
                 for (px = namex[ix], i = 0; *px && *px != ':'; px + +, i+ +)
                           (void) putc(*px, fx);
                 for (; i < lmax + P_SPC; i++)
                           (void) putc(' ', fx);
10
                 /* these count from 1:
                  * ni[] is current element (from 1)
                  * nc[] is number at start of current line
15
                 for (px = out[ix]; *px; px++)
                          (void) putc(*px&0x7F, fx);
                 (void) putc('\n', fx);
        }
20
         * put a line of stars (seqs always in out[0], out[1]): dumpblock()
        static
25
        stars()
                                                                                                                        stars
        {
                                    *p0, *p1, cx, *px;
                 register char
30
                 if (!*out[0] || (*out[0] == ' ' && *(po[0]) == ' ') ||
                    !*out[1] || (*out[1] == ' ' && *(po[1]) == ' '))
                           return;
                 px = star;
                 for (i = lmax + P_SPC; i; i--)
35
                           *px + + = ' ';
                 for (p0 = out[0], p1 = out[1]; *p0 && *p1; p0++, p1++) {
                           if (isalpha(*p0) && isalpha(*p1)) {
40
                                    if (xbm[*p0-'A']&xbm[*p1-'A']) {
    cx = '*';
                                              nm++;
                                    else if (!dna && _day[*p0-'A'][*p1-'A'] > 0)
45
                                              cx = '.\ddot{};
                                    else
                                              cx = ' ';
                           else
50
                                    cx =
                  *px++ = '\n';
                  *px = '\0';
55
        }
```

60

60

```
* strip path or prefix from pn, return len: pr_align()
        static
 5
                                                                                                              stripname
        stripname(pn)
                                   /* file name (may be path) */
                 char
                          *pn;
        {
                 register char
                                   *px, *py;
10
                 py = 0;
                 for (px = pn; *px; px++)

if (*px = = '/')
                                   py = px + 1;
15
                          (void) strcpy(pn, py);
                 return(strlen(pn));
        }
20
25
30
35
40
45
50
55
```

```
* cleanup() -- cleanup any tmp file
          * getseq() -- read in seq, set dna, len, maxlen
          * g_calloc() -- calloc() with error checkin
  5
          * readjmps() -- get the good jmps, from tmp file if necessary
          * writejmps() -- write a filled array of jmps to a tmp file: nw()
         #include "nw.h"
         #include < sys/file.h>
10
         char
                   *jname = "/tmp/homgXXXXXX";
                                                                  /* tmp file for jmps */
         FILE
         int
                  cleanup();
                                                                  /* cleanup tmp file */
15
         long
                  lseek();
          * remove any tmp file if we blow
          */
20
                                                                                                                       cleanup
         cleanup(i)
                  int
                            i;
         {
                  if (fj)
                            (void) unlink(jname);
25
                  exit(i);
         }
          * read, return ptr to seq, set dna, len, maxlen
30
          * skip lines starting with ';', '<', or '>'
          * seq in upper or lower case
          */
         char
         getseq(file, len)
                                                                                                                         getseq
35
                  char
                            *file;
                                     /* file name */
                  int
                                     /* seq len */
         {
                  char
                                     line[1024], *pseq;
                                     *px, *py;
                  register char
40
                  int
                                     natgc, tlen;
                  FILE
                                     *fp;
                  if ((fp = fopen(file, "r")) = = 0) {
                            fprintf(stderr, "%s: can't read %s\n", prog, file);
45
                           exit(1);
                  tlen = natgc = 0;
                  while (fgets(line, 1024, fp)) {
                           if (*line == ';' || *line == '<' || *line == '>')
50
                                     continue;
                           for (px = line; *px != '\n'; px++)
                                     if (isupper(*px) | | islower(*px))
                                              tlen++;
55
                  if ((pseq = malloc((unsigned)(tlen+6))) = = 0) {
                            fprintf(stderr, "%s: malloc() failed to get %d bytes for %s\n", prog, tlen+6, file);
                           exit(1);
                  pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0';
60
```

```
...getseq
                   py = pseq + 4;
                    *len = tlen;
                   rewind(fp);
  5
                   while (fgets(line, 1024, fp)) {
    if (*line == ';' || *line == '<' || *line == '>')
                                      continue;
                             for (px = line; *px != '\n'; px++) {
 10
                                      if (isupper(*px))
                                                *py++ = *px;
                                      else if (islower(*px))
                                                *py++ = toupper(*px);
                                      if (index("ATGCU",*(py-1)))
15
                                                natgc++;
                            }
                    *py++ = '\0';
                   *py = '\0';
20
                   (void) fclose(fp);
                   dna = natgc > (tlen/3);
                   return(pseq+4);
         }
25
         char
                                                                                                                         g_calloc
         g_calloc(msg, nx, sz)
                                                /* program, calling routine */
                   char
                            *msg;
                   int
                                                /* number and size of elements */
                            nx, sz;
         {
30
                   char
                                      *px, *calloc();
                   if ((px = calloc((unsigned)nx, (unsigned)sz)) = = 0) {
                                      fprintf(stderr, "%s: g_calloc() failed %s (n=%d, sz=%d)\n", prog, msg, nx, sz);
35
                            }
                   }
                   return(px);
         }
40
          * get final jmps from dx[] or tmp file, set pp[], reset dmax: main()
                                                                                                                       readjmps
         readjmps()
45
         {
                  int
                                      fd = -1;
                                      siz, i0, i1;
                  register i, j, xx;
50
                  if (fj) {
                            (void) fclose(fj);
                            if ((fd = open(jname, O_RDONLY, 0)) < 0) {
    fprintf(stderr, "%s: can't open() %s\n", prog, jname);</pre>
                                      cleanup(1);
55
                            }
                  for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; ; i++) {
                            while (1) {
                                      for (j = dx[dmax].ijmp; j > = 0 && dx[dmax].jp.x[j] > = xx; j-)
60
```

Table 1 (cont')

...readjmps

```
if (j < 0 && dx[dmax].offset && fj) {
                                                  (void) lseek(fd, dx[dmax].offset, 0);
                                                  (void) read(fd, (char *)&dx[dmax].jp, sizeof(struct jmp));
  5
                                                  (void) read(fd, (char *)&dx[dmax].offset, sizeof(dx[dmax].offset));
                                                  dx[dmax].ijmp = MAXJMP-1;
                                       }
                                       else -
                                                  break;
 10
                             if (i > = JMPS) {
                                       fprintf(stderr, "%s: too many gaps in alignment\n", prog);
                                       cleanup(1);
 15
                             if (j > = 0) {
                                       siz = dx[dmax].jp.n[j];
                                       xx = dx[dmax].jp.x[j];
                                       dmax + = siz;
                                       if (siz < 0) {
                                                                      /* gap in second seq */
20
                                                 pp[1].n[i1] = -siz;
                                                 xx += siz;
                                                 /* id = xx - yy + len1 - 1
                                                  pp[1].x[i1] = xx - dmax + len1 - 1;
25
                                                 gapy++;
                                                 ngapy -= siz;
          /* ignore MAXGAP when doing endgaps */
                                                 siz = (-siz < MAXGAP | | endgaps)? -siz : MAXGAP;
30
                                       else if (siz > 0) { /* gap in first seq */
                                                 pp[0].n[i0] = siz;
                                                 pp[0].x[i0] = xx;
                                                 gapx++;
35
                                                 ngapx += siz;
         /* ignore MAXGAP when doing endgaps */
                                                 siz = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
                                                 i0++;
                                       }
40
                             }
                             else
                                       break;
                   }
45
                   /* reverse the order of jmps
                   for (j = 0, i0-; j < i0; j++, i0--)
                            i = pp[0].n[j]; pp[0].n[j] = pp[0].n[i0]; pp[0].n[i0] = i;

i = pp[0].x[j]; pp[0].x[j] = pp[0].x[i0]; pp[0].x[i0] = i;
50
                   for (j = 0, i1-; j < i1; j++, i1-)
                            i = pp[1].n[j]; pp[1].n[j] = pp[1].n[i1]; pp[1].n[i1] = i;

i = pp[1].x[j]; pp[1].x[j] = pp[1].x[i1]; pp[1].x[i1] = i;
55
                   if (fd > = 0)
                            (void) close(fd);
                   if (fj) {
                            (void) unlink(jname);
                            fj = 0;
60
                            offset = 0;
                   }
                                                           }
```

```
* write a filled jmp struct offset of the prev one (if any): nw()
   5
                                                                                                                                                               writejmps
             writejmps(ix)
                          int
                          char
                                       *mktemp();
 10
                         if (!fj) {
                                      if (mktemp(jname) < 0) {
          fprintf(stderr, "%s: can't mktemp() %s\n", prog, jname);
          cleanup(1);</pre>

}
if ((fj = fopen(jname, "w")) == 0) {
    fprintf(stderr, "%s: can't write %s\n", prog, jname);
}

 15
                                      }
 20
                         (void) fwrite((char *)&dx[ix].jp, sizeof(struct jmp), 1, fj);
(void) fwrite((char *)&dx[ix].offset, sizeof(dx[ix].offset), 1, fj);
            }
 25
30
35
40
45
50
55
60
```

Table 2

PRO XXXXXXXXXXXXXX (Length = 15 amino acids)

Comparison Protein XXXXXYYYYYYYY (Length = 12 amino acids)

5 % amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

10 5 divided by 15 = 33.3%

Table 3

15 PRO XXXXXXXXXX (Length = 10 amino acids)

Comparison Protein XXXXXYYYYYYZZYZ (Length = 15 amino acids)

% amino acid sequence identity =

(the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) =

5 divided by 10 = 50%

Table 4

PRO-DNA

имимимимимими

(Length = 14 nucleotides)

Comparison DNA

NNNNNNLLLLLLLLLL

(Length = 16 nucleotides)

5 % nucleic acid sequence identity =

(the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) =

10 6 divided by 14 = 42.9%

Table 5

15 PRO-DNA

NNNNNNNNNN

(Length = 12 nucleotides)

Comparison DNA

NNNNLLLVV

(Length = 9 nucleotides)

% nucleic acid sequence identity =

20 (the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) =

4 divided by 12 = 33.3%

II. Compositions and Methods of the Invention

A. Full-Length PRO Polypeptides

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The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

B. PRO Polypeptide Variants

In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the native full-length sequence PRO or in various domains of the PRO described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 6 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 6, or as further described below in reference to amino acid classes, are introduced and the products screened.

Table 6

20	Original	Exemplary	Preferred
	<u>Residue</u>	<u>Substitutions</u>	<u>Substitutions</u>
			_
	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
25	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
	Cys (C)	ser	ser
	Gln (Q)	asn	asn
	Glu (E)	asp	asp
30	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
	Ile (I)	leu; val; met; ala; phe;	
		norleucine	leu
	Leu (L)	norleucine; ile; val;	
35		met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
	Met (M)	leu; phe; ile	leu
	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
40	Ser (S)	thr	thr
	Thr (T)	ser	ser
	Trp (W)	tyr; phe	tyr
	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe;	-
45		ala; norleucine	leu

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Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- (1) hydrophobic: norleucine, met, ala, val, leu, ile;
 - (2) neutral hydrophilic: cys, ser, thr;
 - (3) acidic: asp, glu;

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- (4) basic: asn, gln, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- 10 (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., Nucl. Acids Res., 13:4331 (1986); Zoller et al., Nucl. Acids Res., 10:6487 (1987)], cassette mutagenesis [Wells et al., Gene, 34:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London SerA, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W.H. Freeman & Co., N.Y.); Chothia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

C. Modifications of PRO

Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-

octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate.

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Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, <u>Proteins: Structure and Molecular Properties</u>, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, <u>CRC Crit. Rev. Biochem.</u>, pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to

be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an α-tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US Patent No. 5,428,130 issued June 27, 1995.

D. Preparation of PRO

The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); Merrifield, J. Am. Chem.

Soc., 85:2149-2154 (1963)]. In vitro protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be

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PRO.

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1. <u>Isolation of DNA Encoding PRO</u>

DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PROencoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length

Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding PRO is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ³²P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., <u>supra</u>, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

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2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Mammalian Cell Biotechnology: a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl₂, CaPO₄, liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., <u>supra</u>, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., <u>Gene</u>, <u>23</u>:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, <u>Virology</u>, <u>52</u>:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the

method of Van Solingen et al., <u>J. Bact.</u>, <u>130</u>:946 (1977) and Hsiao et al., <u>Proc. Natl. Acad. Sci. (USA)</u>, <u>76</u>:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., <u>Methods in Enzymology</u>, 185:527-537 (1990) and Mansour et al., <u>Nature</u>, 336:348-352 (1988).

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Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as E. coli. Various E. coli strains are publicly available, such as E. coli K12 strain MM294 (ATCC 31,446); E. coli X1776 (ATCC 31,537); E. coli strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as Escherichia, e.g., E. coli, Enterobacter, Erwinia, Klebsiella, Proteus, Salmonella, e.g., Salmonella typhimurium, Serratia, e.g., Serratia marcescans, and Shigella, as well as Bacilli such as B. subtilis and B. licheniformis (e.g., B. licheniformis 41P disclosed in DD 266,710 published 12 April 1989), Pseudomonas such as P. aeruginosa, and Streptomyces. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including E. coli W3110 strain 1A2, which has the complete genotype tonA; E. coli W3110 strain 9E4, which has the complete genotype tonA ptr3; E. coli W3110 strain 27C7 (ATCC 55,244), which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan'; E. coli W3110 strain 37D6, which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan'; E. coli W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant degP deletion mutation; and an E. coli strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, in vitro methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. Saccharomyces cerevisiae is a commonly used lower eukaryotic host microorganism. Others include Schizosaccharomyces pombe (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published 2 May 1985); Kluyveromyces hosts (U.S. Patent No. 4,943,529; Fleer et al., Bio/Technology, 9:968-975 (1991)) such as, e.g., K. lactis (MW98-8C, CBS683, CBS4574; Louvencourt et al., J. Bacteriol., 154(2):737-742 [1983]), K. fragilis (ATCC 12,424), K. bulgaricus (ATCC 16,045), K. wickeramii (ATCC 24,178), K. waltii (ATCC 56,500), K. drosophilarum (ATCC 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), K. thermotolerans, and K. marxianus; yarrowia (EP 402,226); Pichia pastoris (EP 183,070; Sreekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); Candida; Trichoderma reesia (EP 244,234); Neurospora crassa (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); Schwanniomyces such as Schwanniomyces occidentalis (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., Neurospora, Penicillium, Tolypocladium (WO 91/00357 published 10 January 1991), and Aspergillus hosts such as A. nidulans (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al.,

Gene, 26:205-221 [1983]; Yelton et al., <u>Proc. Natl. Acad. Sci. USA</u>, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, <u>EMBO J.</u>, 4:475-479 [1985]). Methylotropic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, <u>The Biochemistry of Methylotrophs</u>, 269 (1982).

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Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as Drosophila S2 and Spodoptera Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

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3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

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The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces* α-factor leaders, the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

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Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for *Bacilli*.

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An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., <u>Proc. Natl. Acad. Sci. USA</u>, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., <u>Nature</u>, 282:39 (1979); Kingsman et al., <u>Gene</u>, 7:141 (1979); Tschemper et al., <u>Gene</u>, 10:157 (1980)]. The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, <u>Genetics</u>, 85:12 (1977)].

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Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the β-lactamase and lactose promoter systems [Chang et al., Nature, 275:615 (1978); Goeddel et al., Nature, 281:544 (1979)], alkaline phosphatase, a tryptophan (trp) promoter system [Goeddel, Nucleic Acids Res., 8:4057 (1980); EP 36,776], and hybrid promoters such as the tac promoter [deBoer et al., Proc. Natl. Acad. Sci. USA, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding PRO.

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Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., <u>J. Biol. Chem.</u>, 255:2073 (1980)] or other glycolytic enzymes [Hess et al., <u>J. Adv. Enzyme Reg.</u>, 7:149 (1968); Holland, <u>Biochemistry</u>, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

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Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

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PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July

1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, α -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in recombinant vertebrate cell culture are described in Gething et al., <u>Nature</u>, 293:620-625 (1981); Mantei et al., <u>Nature</u>, 281:40-46 (1979); EP 117,060; and EP 117,058.

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4. <u>Detecting Gene Amplification/Expression</u>

Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, Proc. Natl. Acad. Sci. USA, 77:5201-5205 (1980)], dot blotting (DNA analysis), or in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

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Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibody epitope.

5. Purification of Polypeptide

Forms of PRO may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, Methods in Enzymology, 182 (1990); Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO produced.

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E. Uses for PRO

Nucleotide sequences (or their complement) encoding PRO have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. PRO nucleic acid will also be useful for the preparation of PRO polypeptides by the recombinant techniques described herein.

The full-length native sequence PRO gene, or portions thereof, may be used as hybridization probes for a cDNA library to isolate the full-length PRO cDNA or to isolate still other cDNAs (for instance, those encoding naturally-occurring variants of PRO or PRO from other species) which have a desired sequence identity to the native PRO sequence disclosed herein. Optionally, the length of the probes will be about 20 to about 50 bases. The hybridization probes may be derived from at least partially novel regions of the full length native nucleotide sequence wherein those regions may be determined without undue experimentation or from genomic sequences including promoters, enhancer elements and introns of native sequence PRO. By way of example, a screening method will comprise isolating the coding region of the PRO gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels, including radionucleotides such as ³²P or ³⁵S, or enzymatic labels such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems. Labeled probes having a sequence complementary to that of the PRO gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to determine which members of such libraries the probe hybridizes to. Hybridization techniques are described in further detail in the Examples below.

Any EST sequences disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

Other useful fragments of the PRO nucleic acids include antisense or sense oligonucleotides comprising a singe-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target PRO mRNA (sense) or PRO DNA (antisense) sequences. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment of the coding region of PRO DNA. Such a fragment generally comprises at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

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Binding of antisense or sense oligonucleotides to target nucleic acid sequences results in the formation of duplexes that block transcription or translation of the target sequence by one of several means, including enhanced degradation of the duplexes, premature termination of transcription or translation, or by other means. The antisense oligonucleotides thus may be used to block expression of PRO proteins. Antisense or sense oligonucleotides further comprise oligonucleotides having modified sugar-phosphodiester backbones (or other sugar linkages, such as those described in WO 91/06629) and wherein such sugar linkages are resistant to endogenous nucleases. Such oligonucleotides with resistant sugar linkages are stable *in vivo* (i.e., capable of resisting enzymatic degradation) but retain sequence specificity to be able to bind to target nucleotide sequences.

Other examples of sense or antisense oligonucleotides include those oligonucleotides which are covalently linked to organic moieties, such as those described in WO 90/10048, and other moieties that increases affinity of the oligonucleotide for a target nucleic acid sequence, such as poly-(L-lysine). Further still, intercalating agents, such as ellipticine, and alkylating agents or metal complexes may be attached to sense or antisense oligonucleotides to modify binding specificities of the antisense or sense oligonucleotide for the target nucleotide sequence.

Antisense or sense oligonucleotides may be introduced into a cell containing the target nucleic acid sequence by any gene transfer method, including, for example, CaPO₄-mediated DNA transfection, electroporation, or by using gene transfer vectors such as Epstein-Barr virus. In a preferred procedure, an antisense or sense oligonucleotide is inserted into a suitable retroviral vector. A cell containing the target nucleic acid sequence is contacted with the recombinant retroviral vector, either *in vivo* or *ex vivo*. Suitable retroviral vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus derived from M-MuLV), or the double copy vectors designated DCT5A, DCT5B and DCT5C (see WO 90/13641).

Sense or antisense oligonucleotides also may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell.

Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. The sense or antisense oligonucleotide-lipid complex is preferably dissociated within the cell by an endogenous lipase.

Antisense or sense RNA or DNA molecules are generally at least about 5 bases in length, about 10 bases in length, about 15 bases in length, about 20 bases in length, about 25 bases in length, about 30 bases in length, about 35 bases in length, about 40 bases in length, about 45 bases in length, about 50 bases in length, about 55 bases in length, about 60 bases in length, about 65 bases in length, about 70 bases in length, about 75 bases in length, about 80 bases in length, about 85 bases in length, about 90 bases in length, about 95 bases in length, about 100 bases in length, or more.

The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO coding sequences.

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Nucleotide sequences encoding a PRO can also be used to construct hybridization probes for mapping the gene which encodes that PRO and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as *in situ* hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

When the coding sequences for PRO encode a protein which binds to another protein (example, where the PRO is a receptor), the PRO can be used in assays to identify the other proteins or molecules involved in the binding interaction. By such methods, inhibitors of the receptor/ligand binding interaction can be identified. Proteins involved in such binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction. Also, the receptor PRO can be used to isolate correlative ligand(s). Screening assays can be designed to find lead compounds that mimic the biological activity of a native PRO or a receptor for PRO. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

Nucleic acids which encode PRO or its modified forms can also be used to generate either transgenic animals or "knock out" animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic animal develops. In one embodiment, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding PRO. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009. Typically, particular cells would be targeted for PRO transgene incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding PRO introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding PRO. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this facet of

the invention, an animal is treated with the reagent and a reduced incidence of the pathological condition, compared to untreated animals bearing the transgene, would indicate a potential therapeutic intervention for the pathological condition.

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Alternatively, non-human homologues of PRO can be used to construct a PRO "knock out" animal which has a defective or altered gene encoding PRO as a result of homologous recombination between the endogenous gene encoding PRO and altered genomic DNA encoding PRO introduced into an embryonic stem cell of the animal. For example, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques. A portion of the genomic DNA encoding PRO can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see e.g., Thomas and Capecchi, Cell, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see e.g., Li et al., Cell, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (e.g., a mouse or rat) to form aggregation chimeras [see e.g., Bradley, in Teratocarcinomas and Embryonic Stem Cells: A Practical Approach, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to absence of the PRO polypeptide.

Nucleic acid encoding the PRO polypeptides may also be used in gene therapy. In gene therapy applications, genes are introduced into cells in order to achieve *in vivo* synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. "Gene therapy" includes both conventional gene therapy where a lasting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes *in vivo*. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik *et al.*, <u>Proc. Natl. Acad. Sci. USA</u> 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro, or in vivo in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in vitro include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred in vivo gene transfer techniques include transfection with viral

(typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau et al., <u>Trends in Biotechnology</u> 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu et al., <u>J. Biol. Chem.</u> 262, 4429-4432 (1987); and Wagner et al., <u>Proc. Natl. Acad. Sci. USA</u> 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson et al., <u>Science</u> 256, 808-813 (1992).

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The PRO polypeptides described herein may also be employed as molecular weight markers for protein electrophoresis purposes and the isolated nucleic acid sequences may be used for recombinantly expressing those markers.

The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

The PRO polypeptides and nucleic acid molecules of the present invention may also be used diagnostically for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another, preferably in a diseased tissue as compared to a normal tissue of the same tissue type. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEENTM, PLURONICSTM or PEG.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

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Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The use of interspecies scaling in toxicokinetics" In Toxicokinetics and New Drug Development, Yacobi et al., Eds., Pergamon Press, New York 1989, pp. 42-96.

When in vivo administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 μ g/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon-(rhIFN-), interleukin-2, and MN rgp120. Johnson et al., Nat. Med., 2:795-799 (1996); Yasuda, Biomed. Ther., 27:1221-1223 (1993); Hora et al., Bio/Technology, 8:755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in Vaccine Design: The Subunit and Adjuvant Approach, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-coglycolic acid (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), <u>Biodegradable Polymers as Drug Delivery Systems</u> (Marcel Dekker: New York, 1990), pp. 1-41.

This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides

encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

All assays for antagonists are common in that they call for contacting the drug candidate with a PRO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

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In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, coimmunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, proteinprotein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, Nature (London), 340:245-246 (1989); Chien et al., Proc. Natl. Acad. Sci. USA, 88:9578-9582 (1991)) as disclosed by Chevray and Nathans, Proc. Natl. Acad. Sci. USA, 89: 5789-5793 (1991). Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-lacZ reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for β-galactosidase. A complete kit (MATCHMAKERTM) for identifying protein-protein interactions between two specific proteins using the twohybrid technique is commercially available from Clontech. This system can also be extended to map protein

domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

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To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., Current Protocols in Immun., 1(2): Chapter 5 (1991). Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a single clone that encodes the putative receptor.

As an alternative approach for receptor identification, labeled PRO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained from micro- sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

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Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res., 6:3073 (1979); Cooney et al., Science, 241: 456 (1988); Dervan et al., Science, 251:1360 (1991)), thereby preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into the PRO polypeptide (antisense - Okano, Neurochem., 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression (CRC Press: Boca Raton, FL, 1988). The oligonucleotides described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of the PRO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiation site, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, <u>Current Biology</u>, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, supra.

These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

Diagnostic and therapeutic uses of the herein disclosed molecules may also be based upon the positive functional assay hits disclosed and described below.

F. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

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2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, <u>Nature</u>, <u>256</u>:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of

HGPRT-deficient cells.

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Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, <u>supra</u>]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., supra] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent

heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

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3. Human and Humanized Antibodies

The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

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Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, <u>J. Mol. Biol.</u>, <u>227</u>:381 (1991); Marks et al., <u>J. Mol. Biol.</u>, <u>222</u>:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., <u>Monoclonal Antibodies and Cancer Therapy</u>, Alan R. Liss, p. 77 (1985) and

Boerner et al., <u>J. Immunol.</u>, <u>147(1)</u>:86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks *et al.*, <u>Bio/Technology 10</u>, 779-783 (1992); Lonberg *et al.*, <u>Nature 368</u> 856-859 (1994); Morrison, <u>Nature 368</u>, 812-13 (1994); Fishwild *et al.*, <u>Nature Biotechnology 14</u>, 845-51 (1996); Neuberger, <u>Nature Biotechnology 14</u>, 826 (1996); Lonberg and Huszar, <u>Intern. Rev. Immunol.</u> <u>13</u> 65-93 (1995).

The antibodies may also be affinity matured using known selection and/or mutagenesis methods as described above. Preferred affinity matured antibodies have an affinity which is five times, more preferably 10 times, even more preferably 20 or 30 times greater than the starting antibody (generally murine, humanized or human) from which the matured antibody is prepared.

4. <u>Bispecific Antibodies</u>

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Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, Nature, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker et al., EMBO <u>I.</u>, 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain.

In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

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Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared can be prepared using chemical linkage. Brennan *et al.*, Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

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Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby *et al.*, J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

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Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

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Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., J. Immunol. 147:60 (1991).

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Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule

on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

5. Heteroconjugate Antibodies

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Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro* using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

6. Effector Function Engineering

It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

7. <u>Immunoconjugates</u>

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolaca americana* proteins

(PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ²¹²Bi, ¹³¹I, ¹³¹In, ⁹⁰Y, and ¹⁸⁶Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is conjugated to a cytotoxic agent (e.g., a radionucleotide).

8. <u>lmmunoliposomes</u>

The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, <u>Proc. Natl. Acad. Sci. USA</u>, <u>82</u>: 3688 (1985); Hwang *et al.*, <u>Proc. Natl. Acad. Sci. USA</u>, <u>77</u>: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No. 5,013,556.

Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin et al., J. Biol. Chem., 257: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon et al., J. National Cancer Inst., 81(19): 1484 (1989).

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9. Pharmaceutical Compositions of Antibodies

Antibodies specifically binding a PRO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

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If the PRO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that

specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, e.g., Marasco et al., Proc. Natl. Acad. Sci. USA, 90: 7889-7893 (1993). The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles, and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT TM (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

G. <u>Uses for anti-PRO Antibodies</u>

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The anti-PRO antibodies of the invention have various utilities. For example, anti-PRO antibodies may be used in diagnostic assays for PRO, e.g., detecting its expression (and in some cases, differential expression) in specific cells, tissues, or serum. Various diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [Zola, Monoclonal Antibodies: A Manual of Techniques, CRC

Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as ³H, ¹⁴C, ³²P, ³⁵S, or ¹²⁵I, a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem, and Cytochem., 30:407 (1982).

Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture or natural sources. In this process, the antibodies against PRO are immobilized on a suitable support, such a Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO from the antibody.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

20 <u>EXAMPLES</u>

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Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

EXAMPLE 1: Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were

often (but not always) extended using repeated cycles of BLAST or BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gcl electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

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1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the Sall/Notl linkered cDNA was cloned into Xhol/Notl cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an Sfil restriction enzyme site preceding the Xhol/Notl cDNA cloning sites.

2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA was sized to 500-1000 bp, linkered with blunt to Notl adaptors, cleaved with Sfil, and cloned into Sfil/Notl cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal) followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

3. Transformation and Detection

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DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL⁺, SUC⁺, GAL⁺. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in sec71, sec72, sec62, with truncated sec71 being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., $\underline{20}$:1425 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about 2 x 10^6 cells/ml (approx. $OD_{600} = 0.1$) into fresh YEPD broth (500 ml) and regrown to 1 x 10^7 cells/ml (approx. $OD_{600} = 0.4$ -0.5).

The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li₂OOCCH₃), and resuspended into LiAc/TE (2.5 ml).

Transformation took place by mixing the prepared cells (100 μ l) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1 μ g, vol. < 10 μ l) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 μ l, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li₂OOCCH₃, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 μ l, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells

were then diluted into TE (1 ml) and aliquots (200 μ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., <u>Methods in Yeast Genetics</u>, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., <u>Anal. Biochem.</u>, <u>172</u>:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

4. Isolation of DNA by PCR Amplification

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When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 μ l) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5 μ l) was used as a template for the PCR reaction in a 25 μ l volume containing: 0.5 μ l Klentaq (Clontech, Palo Alto, CA); 4.0 μ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 μ l Kentaq buffer (Clontech); 0.25 μ l forward oligo 1; 0.25 μ l reverse oligo 2; 12.5 μ l distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAAAACGACGGCCAGT<u>TAAATAGACCTGCAATTATTAATCT</u>-3' (SEQ ID NO:553)
The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACC<u>ACCTGCACACCTGCAAATCCATT</u>-3' (SEQ ID NO:554) PCR was then performed as follows:

30	a.		Denature	92°C,	5 minutes
30	b.	3 cycles of:	Denature Anneal Extend	-	30 seconds 30 seconds 60 seconds
35	c.	3 cycles of:	Denature Anneal Extend		30 seconds 30 seconds 60 seconds
40	d.	25 cycles of:	Denature Anneal Extend	92°C, 55°C, 72°C,	30 seconds 30 seconds 60 seconds

e. Hold 4°C

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 μ l) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., <u>supra</u>. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

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EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO Polypeptides

Using the techniques described in Examples 1 to 3 above, numerous full-length cDNA clones were identified as encoding PRO polypeptides as disclosed herein. These cDNAs were then deposited under the terms of the Budapest Treaty with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC) as shown in Table 7 below.

Table 7

	<u>Material</u>	ATCC Dep. No.	Deposit Date
	DNA16438-1387	209771	April 14, 1998
35	DNA19360-2552	203654	February 9, 1999
	DNA33455-1548	PTA-127	May 25, 1999
	DNA37155-2651	PTA-429	July 27, 1999
	DNA38269-2654	PTA-432	July 27, 1999
	DNA40619-1220	209525	December 10, 1997

		Table 7 (con	<u>t')</u>
_	<u>Material</u>	ATCC Dep. No.	Deposit Date
•	DNA44174-2513	203577	January 12, 1999
	DNA44675-2662	PTA-430	July 27, 1999
	DNA45408-2615	PTA-203	June 8, 1999
5	DNA48606-1479	203040	July 1, 1998
•	DNA52753-2656	PTA-611	August 31, 1999
	DNA53915-1258	209593	January 21, 1998
	DNA53991-2553	203649	February 9, 1999
	DNA54009-2517	203574	January 12, 1999
10	DNA56055-1643	PTA-129	May 25, 1999
10	DNA57033-1403	209905	May 27, 1998
	DNA57252-1453	203585	January 12, 1999
	DNA58799-1652	203665	February 9, 1999
	DNA59770-2652	PTA-427	July 27, 1999
15	DNA59770-2032 DNA59774-2665	PTA-615	August 31, 1999
13	DNA60281-2518	203582	January 12, 1999
	DNA60736-2559	203382	March 9, 1999
		PTA-428	July 27, 1999
	DNA61875-2653		
20	DNA62312-2558	203836 PTA 205	March 9, 1999
20	DNA62849-1604	PTA-205	June 8, 1999
	DNA66307-2661	PTA-431	July 27, 1999
	DNA66677-2535	203659	February 9, 1999
•	DNA71235-1706	203584	January 12, 1999
25	DNA71289-2547	PTA-126	May 25, 1999
25	DNA73775-1707	PTA-128	May 25, 1999
	DNA76385-1692	203664	February 9, 1999
	DNA76395-2527	203578	January 12, 1999
	DNA77622-2516	203554	December 22, 1998
20	DNA77629-2573	203850	March 16, 1999
30	DNA77645-2648	PTA-45	May 11, 1999
	DNA79302-2521	203545	December 22, 1998
	DNA79865-2519	203544	December 22, 1998
	DNA80135-2655	PTA-234	June 15, 1999
25	DNA80794-2568	203848	March 16, 1999
35	DNA80796-2523	203555	December 22, 1998
	DNA80840-2605	203949	April 20, 1999
	DNA80899-2501	203539	December 15, 1998
	DNA81228-2580	203871	March 23, 1999
40	DNA81761-2583	203862	March 23, 1999
40	DNA82358-2738	PTA-510	August 10, 1999
	DNA82364-2538	203603	January 20, 1999
	DNA82424-2566	203813	March 2, 1999
	DNA82430-2557	203812	March 2, 1999
4.5	DNA83500-2506	203391	October 29, 1998
45	DNA83509-2612	203965	April 27, 1999
	DNA83560-2569	203816	March 2, 1999
	DNA84139-2555	203814	March 2, 1999
	DNA84141-2556	203810	March 2, 1999
50	DNA84142-2613	PTA-22	May 4, 1999
50	DNA84318-2520	203580	January 12, 1999
	DNA84909-2590	203889	March 30, 1999
	DNA84912-2610	203964	April 27, 1999
	DNA84925-2514	203548	December 22, 1998
	DNA84928-2564	203817	March 2, 1999
55	DNA84932-2657	PTA-235	June 15, 1999

		<u>l'able / (con</u>	
	<u>Material</u>	ATCC Dep. No.	Deposit Date
	DNA86592-2607	203968	April 27, 1999
	DNA86594-2587	203894	March 30, 1999
	DNA86647-2591	203893	March 30, 1999
5	DNA87185-2563	203811	March 2, 1999
	DNA87656-2582	203867	March 23, 1999
	DNA87974-2609	203963	April 27, 1999
	DNA88001-2565	203815	March 2, 1999
	DNA88004-2575	203890	March 30, 1999
10	DNA89220-2608	PTA-130	May 25, 1999
	DNA89947-2618	203970	April 27, 1999
	DNA90842-2574	203845	March 16, 1999
	DNA91775-2581	203861	March 23, 1999
	DNA91779-2571	203844	March 16, 1999
15	DNA92217-2697	PTA-513	August 10, 1999
	DNA92219-2541	203663	February 9, 1999
	DNA92223-2567	203851	March 16, 1999
	DNA92225-2603	203950	April 20, 1999
	DNA92232-2589	203895	March 30, 1999
20	DNA92233-2599	PTA-134	May 25, 1999
	DNA92243-2549	203852	March 16, 1999
	DNA92253-2671	PTA-258	June 22, 1999
	DNA92254-2672	PTA-259	June 22, 1999
	DNA92255-2584	203866	March 23, 1999
25	DNA92269-2570	203853	March 16, 1999
	DNA92288-2588	203892	March 30, 1999
	DNA92290-2550	203847	March 16, 1999
	DNA93012-2622	PTA-21	May 4, 1999
	DNA93020-2642	PTA-121	May 25, 1999
30	DNA94830-2604	203951	April 20, 1999
	DNA94833-2579	203869	March 23, 1999
	DNA94838-2658	PTA-232	June 15, 1999
	DNA94844-2686	PTA-385	July 20, 1999
	DNA94854-2586	203864	March 23, 1999
35	DNA96868-2677	PTA-262	June 22, 1999
	DNA96871-2683	PTA-381	July 20, 1999
	DNA96880-2624	PTA-15	May 4, 1999
	DNA96986-2660	PTA-239	June 15, 1999
	DNA96988-2685	PTA-384	July 20, 1999
40	DNA96995-2709	PTA-475	August 3, 1999
	DNA97004-2562	203854	March 16, 1999
	DNA97005-2687	PTA-378	July 20, 1999
	DNA97009-2668	PTA-257	June 22, 1999
	DNA97013-2667	PTA-231	June 15, 1999
45	DNA98380-2690	PTA-388	July 20, 1999
	DNA98561-2696	PTA-620	August 31, 1999
	DNA98575-2644	PTA-118	May 25, 1999
	DNA98593-2694	PTA-477	August 3, 1999
	DNA98600-2703	PTA-488	August 3, 1999
50	DNA99391-2572	203849	March 16, 1999
	DNA99393-2560	203837	March 9, 1999
	DNA100276-2684	PTA-380	July 20, 1999
	DNA100312-2645	PTA-44	May 11, 1999
	DNA100902-2646	PTA-42	May 11, 1999
55	DNA102899-2679	PTA-123	May 25, 1999

		Table / (con	<u>r)</u>
	<u>Material</u>	ATCC Dep. No.	Deposit Date
	DNA104875-2720	PTA-482	August 3, 1999
	DNA105680-2710	PTA-483	August 3, 1999
	DNA105779-2708	PTA-485	August 3, 1999
5	DNA105794-2695	PTA-480	August 3, 1999
	DNA105838-2702	PTA-476	August 3, 1999
	DNA107698-2715	PTA-472	August 3, 1999
	DNA107701-2711	PTA-487	August 3, 1999
	DNA107781-2707	PTA-484	August 3, 1999
10	DNA108670-2744	PTA-546	August 17, 1999
	DNA108688-2725	PTA-515	August 10, 1999
	DNA108769-2765	PTA-861	October 19, 1999
	DNA108935-2721	PTA-518	August 10, 1999
	DNA110700-2716	PTA-512	August 10, 1999
15	DNA111750-2706	PTA-489	August 3, 1999
15	DNA123430-2755	PTA-614	August 31, 1999
	DNA125154-2785	PTA-957	November 16,1999
	DNA142238-2768	PTA-819	October 5, 1999
	DNA22779-1130	209280	September 18, 1997
20	DNA26847-1395	209772	April 14, 1998
20	DNA27864-1155	209375	October 16, 1997
	DNA27865-1091	209296	September 23, 1997
	DNA28497-1130	209279	September 18, 1997
	DNA29101-1122	209653	March 5, 1998
25	DNA32286-1191	209335	October 16, 1997
23	DNA32288-1132	209261	September 16, 1997
	DNA32290-1164	209384	October 16, 1997
	DNA32292-1131	209258	September 16, 1997
	DNA32298-1132	209257	September 16, 1997
30	DNA33085-1110	209087	May 30, 1997
50	DNA33087-1158	209381	October 16, 1997
	DNA33089-1132	209262	September 16, 1997
	DNA33092-1202	209420	October 28, 1997
	DNA33094-1131	209256	September 16, 1997
35	DNA33107-1135	209251	September 16, 1997
J.	DNA33221-1133	209263	September 16, 1997
	DNA33223-1136	209264	September 16, 1997
	DNA33460-1166	209376	October 16, 1997
	DNA33473-1176	209391	October 17, 1997
40	DNA33785-1143	209417	October 28, 1997
	DNA33786-1132	209253	September 16, 1997
	DNA34353-1428	209855	May 12, 1998
	DNA34392-1170	209526	December 10, 1997
	DNA34434-1139	209252	September 16, 1997
45	DNA35558-1167	209374	October 16, 1997
	DNA35595-1228	209528	December 10, 1997
	DNA35638-1216	209265	September 16, 1997
	DNA35639-1172	209396	October 17, 1997
	DNA35663-1129	209201	August 18, 1997
50	DNA35674-1142	209416	October 28, 1997
	DNA35841-1173	209403	October 17, 1997
	DNA35916-1161	209419	October 28, 1997
	DNA35918-1174	209402	October 17, 1997
	DNA36350-1158	209378	October 16, 1997
55	DNA37140-1234	209489	November 21, 1997

		Table 7 (con	<u>:')</u>
	<u>Material</u>	ATCC Dep. No.	Deposit Date
	DNA37150-1178	209401	October 17, 1997
	DNA38260-1180	209397	October 17, 1997
	DNA40021-1154	209389	October 17, 1997
5	DNA40587-1231	209438	November 7, 1997
	DNA40592-1242	209492	November 21, 1997
	DNA40620-1183	209388	October 17, 1997
	DNA40628-1216	209432	November 7, 1997
	DNA40981-1234	209439	November 7, 1997
10	DNA40982-1235	209433	November 7, 1997
	DNA41234-1242	209618	February 5, 1998
	DNA43046-1225	209484	November 21, 1997
	DNA43316-1237	209487	November 21, 1997
	DNA44167-1243	209434	November 7, 1997
15	DNA44184-1319	209704	March 26, 1998
	DNA44194-1317	209808	April 28, 1998
	DNA44196-1353	209847	May 6, 1998
	DNA45419-1252	209616	February 5, 1998
	DNA46777-1253	209619	February 5, 1998
20	DNA47394-1572	203109	August 11, 1998
	DNA48331-1329	209715	March 31, 1998
	DNA48336-1309	209669	March 11, 1998
	DNA49142-1430	203002	June 23, 1998
	DNA49646-1327	209705	March 26, 1998
25	DNA49821-1562	209981	June 16, 1998
	DNA49829-1346	209749	April 7, 1998
	DNA50921-1458	209859	May 12, 1998
	DNA52187-1354	209845	May 6, 1998
	DNA52196-1348	209748	April 7, 1998
30	DNA52598-1518	203107	August 11, 1998
	DNA54228-1366	209801	April 23, 1998
	DNA56047-1456	209948	June 9, 1998
	DNA56112-1379	209883	May 20, 1998
	DNA56113-1378	203049	July 1, 1998
35	DNA56352-1358	209846	May 6, 1998
	DNA56433-1406	209857	May 12, 1998
	DNA56439-1376	209864	May 14, 1998
	DNA57530-1375	209880	May 20, 1998
40	DNA57689-1385	209869	May 14, 1998
40	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
	DNA58721-1475	203110	August 11, 1998
46	DNA59205-1421	203009	June 23, 1998
45	DNA59215-1425	209961	June 9, 1998
	DNA59220-1514	209962	June 9, 1998
	DNA59294-1381	209866	May 14, 1998
	DNA59488-1603	203157	August 25, 1998
50	DNA59588-1571	203106	August 11, 1998
50	DNA59606-1471	209945	June 9, 1998
	DNA59620-1463	209989	June 16, 1998
	DNA59767-1489	203108	August 11, 1998
	DNA59777-1480	203111	August 11, 1998
55	DNA59814-1486	203359	October 20, 1998
55	DNA59839-1461	209988	June 16, 1998

Table 7 (cont')

		Table 7 (cont')		
	<u>Material</u>	ATCC Dep. No.	Deposit Date	
	DNA59846-1503	209978	June 16, 1998	
	DNA59847-1511	203098	August 4, 1998	
	DNA60615-1483	209980	June 16, 1998	
5	DNA60621-1516	203091	August 4, 1998	
	DNA60622-1525	203090	August 4, 1998	
	DNA60627-1508	203092	August 4, 1998	
	DNA60764-1533	203452	November 10, 1998	
	DNA60775-1532	203173	September 1, 1998	
10	DNA61185-1646	203464	November 17, 1998	
	DNA61873-1574	203132	August 18, 1998	
	DNA62306-1570	203254	September 9, 1998	
	DNA62808-1582	203358	October 20, 1998	
	DNA62814-1521	203093	August 4, 1998	
15	DNA64885-1529	203457	November 3, 1998	
	DNA64886-1601	203241	September 9, 1998	
	DNA64888-1542	203249	September 9, 1998	
	DNA64889-1541	203250	September 9, 1998	
	DNA64890-1612	203131	August 18, 1998	
20	DNA64903-1553	203223	September 15, 1998	
	DNA64905-1558	203233	September 15, 1998	
	DNA65402-1540	203252	September 9, 1998	
	DNA65405-1547	203476	November 17, 1998	
	DNA65412-1523	203094	August 4, 1998	
25	DNA66309-1538	203235	September 15, 1998	
	DNA66667-1596	203267	September 22, 1998	
	DNA66675-1587	203282	September 22, 1998	
	DNA68818-2536	203657	February 9, 1999	
	DNA68864-1629	203276	September 22, 1998	
30	DNA68872-1620	203160	August 25, 1998	
	DNA71159-1617	203135	August 18, 1998	
	DNA73727-1673	203459	November 3, 1998	
	DNA73739-1645	203270	September 22, 1998	
0.5	DNA76400-2528	203573	January 12, 1999	
35	DNA76510-2504	203477	November 17, 1998	
	DNA76529-1666	203315	October 6, 1998	
	DNA76538-1670	203313	October 6, 1998	
	DNA77301-1708	203407	October 27, 1998	
40 .	DNA77624-2515	203553	December 22, 1998	
40	DNA79230-2525	203549	December 22, 1998	
	DNA79862-2522	203550	December 22, 1998	
	DNA80145-2594	PTA-204	June 8, 1999	
	DNA83500-2506	203391	October 29, 1998	
15	DNA84917-2597	203863	March 23, 1999	
45	DNA92218-2554	203834	March 9, 1999	
	DNA96042-2682	PTA-382	July 20, 1999	

These deposits were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of

the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).

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The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

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EXAMPLE 5: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

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Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

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DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 6: Expression of PRO in E. coli

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This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in E. coli.

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The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

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The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., <u>supra</u>. Transformants are identified by their ability to grow on LB plates and antibiotic resistant

colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

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PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H2O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4 °C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the

solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

15 EXAMPLE 7: Expression of PRO in mammalian cells

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This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., <u>supra</u>. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μ g pRK5-PRO DNA is mixed with about 1 μ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 μ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μ Ci/ml ³⁵S-cysteine and 200 μ Ci/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μ g/ml bovine insulin and 0.1 μ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

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In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a polyhis tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., <u>Current Protocols of Molecular Biology</u>, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., <u>Nucl. Acids Res.</u> 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect* (Quiagen), Dosper* or Fugene* (Boehringer

Mannheim). The cells are grown as described in Lucas et al., <u>supra</u>. Approximately 3×10^{-7} cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3 x 105 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2 x 106 cells/mL. On day 0, the cell number pH ie determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 8: Expression of PRO in Yeast

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The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme

sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 9: Expression of PRO in Baculovirus-Infected Insect Cells

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The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold[™] virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., <u>Baculovirus expression vectors: A Laboratory Manual</u>, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM

phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni^{2+} -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His_{10} -tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 10: Preparation of Antibodies that Bind PRO

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This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, <u>supra</u>. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

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EXAMPLE 11: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSETM (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 12: Drug Screening

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This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (I) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment

and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 13: Rational Drug Design

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The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (i.e., a PRO polypeptide) or of small molecules with which they interact, e.g., agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide in vivo (c.f., Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda et al., J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then

be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

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EXAMPLE 14: Identification of PRO Polypeptides That Stimulate TNF-α Release In Human Blood (Assay 128)

This assay shows that certain PRO polypeptides of the present invention act to stimulate the release of TNF- α in human blood. PRO polypeptides testing positive in this assay are useful for, among other things, research purposes where stimulation of the release of TNF- α would be desired and for the therapeutic treatment of conditions wherein enhanced TNF- α release would be beneficial. Specifically, 200 μ l of human blood supplemented with 50mM Hepes buffer (pH 7.2) is aliquoted per well in a 96 well test plate. To each well is then added 300 μ l of either the test PRO polypeptide in 50 mM Hepes buffer (at various concentrations) or 50 mM Hepes buffer alone (negative control) and the plates are incubated at 37°C for 6 hours. The samples are then centrifuged and 50 μ l of plasma is collected from each well and tested for the presence of TNF- α by ELISA assay. A positive in the assay is a higher amount of TNF- α in the PRO polypeptide treated samples as compared to the negative control samples.

The following PRO polypeptides tested positive in this assay: PRO195, PRO202, PRO215, PRO221, PRO217, PRO222, PRO198, PRO245, PRO172, PRO265, PRO266, PRO344, PRO337, PRO322, PRO1286, PRO1279, PRO1338 and PRO1343.

EXAMPLE 15: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as being capable of affecting glucose and/or FFA uptake by skeletal muscle in this assay: PRO182, PRO366, PRO198, PRO172 and PRO719.

EXAMPLE 16: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articulary cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 μ g/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 μ l of the same media without serum and 100 μ l of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μ l/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO182, PRO366, PRO198 and PRO1868.

EXAMPLE 17: Chondrocyte Proliferation Assay (Assay 111)

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This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

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Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 μ g/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm² every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 μ l of the same media without serum and 100 μ l of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 μ l/well. After 5 days at 37°C, 20 μ l of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 μ l of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

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The following PRO polypeptides tested positive in this assay: PRO202, PRO224, PRO172 and PRO1312.

EXAMPLE 18: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

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This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes

would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as being capable of affecting glucose and/or FFA uptake in this assay: PRO202, PRO211, PRO344 and PRO1338.

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EXAMPLE 19: Gene Expression in Bovine Pericytes (Assay 105)

This assay is designed to identify PRO polypeptides which activate gene expression in pericytes. Such polypeptides would be expected to be useful as growth factors and/or for situations where the activation of gene expression is desired or beneficial. Bovine pericytes are plated on 60mm culture dishes in growth media for 1 week. On day 1, various PRO polypeptides are diluted (1%) and incubated with the pericytes for 1, 4 and 24 hr. timepoints. The cells are harvested and the RNA isolated using TRI-Reagent following the included instructions. The RNA is then quantified by reading the 260/280 OD using a spectrophotometer. The gene expression analysis is done by TaqMan reactions using Perkin Elmer reagents and specially designed bovine probes and primers. Expression of the following genes is analyzed: GAPDH, beta-integrin, connective tissue growth factor (CTGF), ICAM-1, monocyte chemoattractant protein-1 (MCP-1), osteopontin, transforming growth factor-beta (TGF-beta), TGF-beta receptor, tissue inhibitor of metalloproteinase (TIMP), tissue factor (TF), VEGF-α, thrombospondin, VEGF-β, angiopoeitin-2, and collagenase. Replicates are then averaged and the SD determined. The gene expression levels are then normalized to GAPDH. These are then normalized to the expression levels obtained with a protein (PIN32) which does not significantly induce gene expression in bovine pericytes when compared to untreated controls. Any PRO polypeptide that gives a gene expression level 2-fold or higher over the PIN32 control is considered a positive hit.

The following PRO polypeptides tested positive in this assay: PRO366.

EXAMPLE 20: Identification of PRO Polypeptides That Activate Pericytes (Assay 125)

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This assay shows that certain polypeptides of the invention act to activate proliferation of pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Such PRO polypeptides also would be expected to be useful as growth factors and/or for situations where the induction of cell proliferation is desired or beneficial. Activation of pericyte proliferation also correlates with the induction of angiogenesis and, as such, PRO polypeptides capable of inducing pericyte proliferation would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing, and the like. Specifically, on day 1, pericytes are received

from VEC Technologies, and all but 5 ml media is removed from the flask. On day 2, the pericytes are trypsinized, washed, spun and plated on 96 well plates. On day 7, the media is removed and the pericytes are treated with $100 \mu l$ of either the specific PRO polypeptide or control treatments (positive control = DME+5%+/-PDGF@500ng/ μl ; negative control=PIN32, a polypeptide determined to have no significant effect on pericyte proliferation). C-fos and GAPDH gene expression levels are then determined and the replicates are averaged and the SD is determined. The c-fos values are normalized to GAPDH and the results are expressed as fold increase over PIN32. Anything providing at least a 2-fold or higher response as compared to the negative control is considered positive for the assay.

The following polypeptides tested positive in this assay: PRO366.

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EXAMPLE 21: Ability of PRO Polypeptides to Stimulate the Release of Proteoglycans from Cartilage (Assay 97)

The ability of various PRO polypeptides to stimulate the release of proteoglycans from cartilage tissue was tested as follows.

The metacarphophalangeal joint of 4-6 month old pigs was aseptically dissected, and articular cartilage was removed by free hand slicing being careful to avoid the underlying bone. The cartilage was minced and cultured in bulk for 24 hours in a humidified atmosphere of 95% air, 5% CO₂ in serum free (SF) media (DME/F121:1) with 0.1% BSA and 100U/ml penicillin and 100μg/ml streptomycin. After washing three times, approximately 100 mg of articular cartilage was aliquoted into micronics tubes and incubated for an additional 24 hours in the above SF media. PRO polypeptides were then added at 1% either alone or in combination with 18 ng/ml interleukin-1α, a known stimulator of proteoglycan release from cartilage tissue. The supernatant was then harvested and assayed for the amount of proteoglycans using the 1,9-dimethyl-methylene blue (DMB) colorimetric assay (Farndale and Buttle, Biochem, Biophys, Acta 883:173-177 (1985)). A positive result in this assay indicates that the test polypeptide will find use, for example, in the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis.

When various PRO polypeptides were tested in the above assay, the polypeptides demonstrated a marked ability to stimulate release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin- 1α and at 24 and 72 hours after treatment, thereby indicating that these PRO polypeptides are useful for stimulating proteoglycan release from cartilage tissue. As such, these PRO polypeptides are useful for the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis. The polypeptides testing positive in this assay are: PRO216.

EXAMPLE 22: Proliferation of Rat Utricular Supporting Cells (Assay 54)

This assay shows that certain polypeptides of the invention act as potent mitogens for inner ear supporting cells which are auditory hair cell progenitors and, therefore, are useful for inducing the regeneration of auditory hair cells and treating hearing loss in mammals. The assay is performed as follows. Rat UEC-4 utricular epithelial cells are aliquoted into 96 well plates with a density of 3000 cells/well in 200 μ l of serum-containing medium at 33°C. The cells are cultured overnight and are then switched to serum-free medium at

 37° C. Various dilutions of PRO polypeptides (or nothing for a control) are then added to the cultures and the cells are incubated for 24 hours. After the 24 hour incubation, 3 H-thymidine (1 μ Ci/well) is added and the cells are then cultured for an additional 24 hours. The cultures are then washed to remove unincorporated radiolabel, the cells harvested and Cpm per well determined. Cpm of at least 30% or greater in the PRO polypeptide treated cultures as compared to the control cultures is considered a positive in the assay.

The following polypeptides tested positive in this assay: PRO172.

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EXAMPLE 23: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO₂) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50: I of irradiated stimulator cells, and

50: I of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO₂ for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x107 cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO344.

EXAMPLE 24: Pericyte c-Fos Induction (Assay 93)

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This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Induction of c-fos expression in pericytes is also indicative of the induction of angiogenesis and, as such, PRO polypeptides capable of inducing the expression of c-fos would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing, and the like. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100 μ l of PRO polypeptide test samples and controls (positive control = DME+5% serum +/- PDGF at 500 ng/ml; negative control = protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading verses frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media = low glucose DMEM = 20% FBS + 1X pen strep + 1X fungizone. Assay Media = low glucose DMEM +5% FBS.

The following polypeptides tested positive in this assay: PRO301, PRO619, PRO1066 and PRO1265.

20 EXAMPLE 25: Cytokine Release Assay (Assay 120)

This assay is designed to determine whether PRO polypeptides of the present invention are capable of inducing the release of cytokines from peripheral blood mononuclear cells (PBMCs). PRO polypeptides capable of inducing the release of cytokines from PBMCs are useful from the treatment of conditions which would benefit from enhanced cytokine release and will be readily evident to those of ordinary skill in the art. Specifically, 1x106 cells/ml of peripheral blood mononuclear cells (PBMC) are cultured with 1% of a PRO polypeptide for 3 days in complete RPMI media. The supernatant is then harvested and tested for increased concentrations of various cytokines by ELISA as compared to a human IgG treated control. A positive in the assay is a 10-fold or greater increase in cytokine concentration in the PRO polypeptide treated sample as compared to the human IgG treated control.

The following polypeptides tested positive in this assay: PRO526 and PRO1343.

EXAMPLE 26: Inhibition of A-Peptide Binding to Factor VIIA (Assay 118)

This assay is designed to identify PRO polypeptides which are capable of inhibiting the binding of A-peptide to factor VIIA, thereby affecting the blood coagulation cascade. PRO polypeptides testing positive in this assay are expected to be useful for the treatment of conditions where alteration of the blood coagulation cascade would be beneficial including, for example, stroke, heart attack and various coagulation disorders. These PRO polypeptides are also useful for the identification of agonist and antagonist molecules which would

also be useful for treatment of those conditions.

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Specifically, 384 well plates are coated with soluble factor VIIA and are incubated overnight at 4° C. The wells are then decanted and are blocked by the addition of 0.5% BSA for 1 hour. The wells are then washed and 20μ l of biotinylated A-peptide and either various concentration of the PRO polypeptide (test) or nothing (negative control) are added to each well. The plates are then incubated for 1 hour at room temperature. The wells are again washed and then 40μ l of streptavidin-europium is added to each well. The plates are then incubated for 30 minutes at room temperature and then washed. 40μ l of a fluorescence enhancement solution is then added to each well, the plates incubated for 5 minutes at room temperature and each well is then read on Wallac Victor reader under europium delayed fluorescence settings. Percent inhibition of binding of the A-peptide to the factor VIIA is then determined (as compared to the negative control), wherein a positive in the assay is a percent inhibition of 30% or greater.

The following PRO polypeptides tested positive in this assay: PRO182.

EXAMPLE 27: Inhibition of Adipocyte Differentiation Assay (Assay 66)

This assay is designed to identify PRO polypeptides which are capable of inhibiting insulin-induced differentiation of adipocytes. PRO polypeptides testing positive in this assay would be expected to be useful for the treatment of conditions associated with obesity, diabetes, etc.

Specifically, 3T3-L1 cells are seeded into the wells of 96 well plates at $6x10^4$ cells/well and allowed to grow to confluency for 7 days. At day 7, the cells are treated with various concentrations of the PRO polypeptide (or nothing for the negative control) in the presence of $1\mu g/ml$ insulin, $0.25x10^6$ M dexamethasone and 0.5mM IBMX. The samples are then incubated at 37°C in 7% CO₂ for 2 days. After the incubation, the media is removed by aspiration and the cells are washed with PBS and re-exposed to the PRO polypeptide (or nothing for the negative control) and $1\mu g/ml$ insulin. After 5 days, the media is removed and replaced with fresh PRO polypeptide (or nothing for the negative control) and insulin. After 5 days, the cells are lysed and the cell lysate is assayed using Sigma's Triglyceride [INT] kit (Sigma procedure #336). A positive in the assay is 20% greater inhibition of adipocyte differentiation in the PRO polypeptide treated samples as compared to the negative control.

The following PRO polypeptides tested positive in this assay: PRO185 and PRO198.

EXAMPLE 28: HUVEC Stimulation by PRO Polypeptides (Assay 131)

This assay is designed to identify PRO polypeptides which are capable of stimulating the proliferation of HUVEC cells. PRO polypeptides testing positive in this assay would be expected to be useful for inducing angiogenesis for the treatment of conditions where angiogenesis would be beneficial including, for example, wound healing, and the like. Antagonists of these PRO polypeptides would be expected to be useful for inhibiting angiogenesis for the treatment of, for example, tumors, and the like.

Specifically, COSTAR® flat bottom black plates are treated with fibronectin for 20 minutes and then washed twice with PBS. HUVEC cells are then plated at 2000 cells/well in an appropriate growth medium. The plates are then incubated overnight and then the PRO polypeptide (1% final concentration), nothing (negative

control) or IL1 β (3.3 ng/ml final concentration; positive control) is added. The plates are again incubated overnight, stained with ICAM1-Cy5 and read on FMAT. A positive in the assay is a 2-fold or greater increase in fluorescence as compared to the positive control.

The following PRO polypeptides tested positive in this assay: PRO222.

EXAMPLE 29: Promotion of Chondrocyte Redifferentiation (Assay 129)

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obtained by the negative control).

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 μ g/ml gentamycin. The culture media is changed every third day. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100μ l of the same media without serum and $100~\mu$ l of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of $200~\mu$ l/well. After 5 days at 37° C, 22 μ l of media comtaining 100μ g/ml Hoechst 33342 and $50~\mu$ g/ml 5-CFDA is added to each well and incubated for an additional 10 minutes at 37° C. A picture of the green fluorescence is taken for each well and the differentiation state of the chondrocytes is calculated by morphometric analysis. A positive result in the assay is obtained when the >50% of the PRO polypeptide treated cells are differentiated (compared to the background

The following PRO polypeptides tested positive in this assay: PRO301.

EXAMPLE 30: Microarray Analysis to Detect Overexpression of PRO Polypeptides in Cancerous Tumors

Nucleic acid microarrays, often containing thousands of gene sequences, are useful for identifying differentially expressed genes in diseased tissues as compared to their normal counterparts. Using nucleic acid microarrays, test and control mRNA samples from test and control tissue samples are reverse transcribed and labeled to generate cDNA probes. The cDNA probes are then hybridized to an array of nucleic acids immobilized on a solid support. The array is configured such that the sequence and position of each member of the array is known. For example, a selection of genes known to be expressed in certain disease states may be arrayed on a solid support. Hybridization of a labeled probe with a particular array member indicates that the sample from which the probe was derived expresses that gene. If the hybridization signal of a probe from a test (disease tissue) sample is greater than hybridization signal of a probe from a control (normal tissue) sample, the gene or genes overexpressed in the disease tissue are identified. The implication of this result is that an overexpressed protein in a diseased tissue is useful not only as a diagnostic marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition.

The methodology of hybridization of nucleic acids and microarray technology is well known in the art. In the present example, the specific preparation of nucleic acids for hybridization and probes, slides, and

hybridization conditions are all detailed in U.S. Provisional Patent Application Serial No. 60/193,767, filed on March 31, 2000 and which is herein incorporated by reference.

In the present example, cancerous tumors derived from various human tissues were studied for PRO polypeptide-encoding gene expression relative to non-cancerous human tissue in an attempt to identify those PRO polypeptides which are overexpressed in cancerous tumors. Two sets of experimental data were generated. In one set, cancerous human colon tumor tissue and matched non-cancerous human colon tumor tissue from the same patient ("matched colon control") were obtained and analyzed for PRO polypeptide expression using the above described microarray technology. In the second set of data, cancerous human tumor tissue from any of a variety of different human tumors was obtained and compared to a "universal" epithelial control sample which was prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung. mRNA isolated from the pooled tissues represents a mixture of expressed gene products from these different tissues. Microarray hybridization experiments using the pooled control samples generated a linear plot in a 2-color analysis. The slope of the line generated in a 2-color analysis was then used to normalize the ratios of (test:control detection) within each experiment. The normalized ratios from various experiments were then compared and used to identify clustering of gene expression. Thus, the pooled "universal control" sample not only allowed effective relative gene expression determinations in a simple 2-sample comparison, it also allowed multi-sample comparisons across several experiments.

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In the present experiments, nucleic acid probes derived from the herein described PRO polypeptideencoding nucleic acid sequences were used in the creation of the microarray and RNA from the tumor tissues listed above were used for the hybridization thereto. A value based upon the normalized ratio:experimental ratio was designated as a "cutoff ratio". Only values that were above this cutoff ratio were determined to be significant. Table 8 below shows the results of these experiments, demonstrating that various PRO polypeptides of the preent invention are significantly overexpressed in various human tumor tissues as compared to a noncancerous human tissue control. As described above, these data demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more cancerous tumors, but also serve as therapeutic targets for the treatment of those tumors.

Table 8

	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO177	breast tumor	universal normal control
30	PRO177	liver tumor	universal normal control
	PRO177	lung tumor	universal normal control
	PRO3574	breast tumor	universal normal control
	PRO3574	colon tumor	matched normal colon control
35	PRO1280	breast tumor	universal normal control
	PRO1280	lung tumor	universal normal control
	PRO4984	lung tumor	universal normal control
	PRO4988	colon tumor	universal normal control
	PRO4988	lung tumor	universal normal control
40	PRO305	lung tumor	universal normal control
	PRO305	colon tumor	universal normal control
	PRO1866	prostate tumor	universal normal control

		Table 8 (cont.)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO1866	lung tumor	universal normal control
	PRO1866	colon tumor	universal normal control
	PRO4996	breast tumor	universal normal control
5	PRO4996	lung tumor	universal normal control
	PRO4406	lung tumor	universal normal control
	PRO4406	colon tumor	universal normal control
	PRO1120	colon tumor	universal normal control
	PRO1120	breast tumor	universal normal control
10	PRO1120	rectal tumor	universal normal control
	PRO4990	lung tumor	universal normal control
	PRO738	cervical tumor	universal normal control
	PRO738	lung tumor	universal normal control
	PRO738	breast tumor	universal normal control
15	PRO3577	lung tumor	universal normal control
10	PRO1879	breast tumor	universal normal control
	PRO1879	lung tumor	universal normal control
	PRO1879	colon tumor	universal normal control
	PRO1471	lung tumor	universal normal control
20	PRO1076	prostate tumor	universal normal control
20	PRO1483	lung tumor	universal normal control
	PRO4985	rectal tumor	universal normal control
	PRO4985	colon tumor	universal normal control
	PRO4985	breast tumor	universal normal control
25	PRO4985	lung tumor	universal normal control
20	PRO5000	lung tumor	universal normal control
	PRO1881	liver tumor	universal normal control
	PRO1881	lung tumor	universal normal control
	PRO1881	breast tumor	universal normal control
30	PRO4314	lung tumor	universal normal control
	PRO4314	breast tumor	universal normal control
	PRO4987	lung tumor	universal normal control
	PRO4313	lung tumor	universal normal control
	PRO4313	breast tumor	universal normal control
35	PRO4799	colon tumor	universal normal control
	PRO4995	liver tumor	universal normal control
	PRO4995	colon tumor	universal normal control
	PRO4995	colon tumor	matched normal colon control
	PRO1341	prostate tumor	universal normal control
40	PRO1341	lung tumor	universal normal control
	PRO1341	colon tumor	universal normal control
	PRO1341	colon tumor	matched normal colon control
	PRO1777	lung tumor	universal normal control
	PRO1777	colon tumor	matched normal colon control
45	PRO3580	lung tumor	universal normal control
	PRO3580	prostate tumor	universal normal control
	PRO1779	lung tumor	universal normal control
	PRO1779	colon tumor	universal normal control
	PRO1779	cervical tumor	universal normal control
50	PRO1754	breast tumor	universal normal control
	PRO1754	lung tumor	universal normal control
	PRO1906	breast tumor	universal normal control
	PRO1906	colon tumor	universal normal control
	PRO1906	prostate tumor	universal normal control
55	PRO1870	breast tumor	universal normal control

		Table 8 (cont')	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO4329	lung tumor	universal normal control
	PRO4979	colon tumor	universal normal control
	PRO1885	rectal tumor	universal normal control
5	PRO1885	colon tumor	universal normal control
	PRO1885	colon tumor	matched normal colon control
	PRO1882	prostate tumor	universal normal control
	PRO1882	lung tumor	universal normal control
	PRO1882	colon tumor	universal normal control
10	PRO1882	breast tumor	universal normal control
	PRO1882	cervical tumor	universal normal control
	PRO4989	rectal tumor	universal normal control
	PRO4989	breast tumor	universal normal control
	PRO4989	colon tumor	matched normal colon control
15	PRO4989	colon tumor	universal normal control
15	PRO4323	lung tumor	universal normal control
	PRO4323	liver tumor	universal normal control
	PRO1886	breast tumor	universal normal control
	PRO1886		universal normal control
20	PRO1886	lung tumor rectal tumor	universal normal control
20	PRO4395	colon tumor	universal normal control
	PRO4395	prostate tumor	universal normal control
	PRO4395	lung tumor	universal normal control
	PRO4395	cervical tumor	universal normal control
25	PRO1782	colon tumor	universal normal control
23	PRO1782	lung tumor	universal normal control
	PRO4388	lung tumor	universal normal control
	PRO4341	breast tumor	universal normal control
	PRO4341	lung tumor	universal normal control
30	PRO3438	lung tumor	universal normal control
	PRO4321	breast tumor	universal normal control
	PRO4321	lung tumor	universal normal control
	PRO4321	colon tumor	universal normal control
	PRO4304	breast tumor	universal normal control
35	PRO4304	lung tumor	universal normal control
	PRO4403	colon tumor	universal normal control
	PRO4403	breast tumor	universal normal control
	PRO4403	lung tumor	universal normal control
	PRO4324	lung tumor	universal normal control
40	PRO4324	breast tumor	universal normal control
	PRO4303	cervical tumor	universal normal control
	PRO4303	lung tumor	universal normal control
	PRO4303	breast tumor	universal normal control
	PRO4303	colon tumor	universal normal control
45	PRO4303	prostate tumor	universal normal control
	PRO4305	breast tumor	universal normal control
	PRO4305	lung tumor	universal normal control
	PRO4305	colon tumor	universal normal control
	PRO4305	liver tumor	universal normal control
50	PRO4404	lung tumor	universal normal control
	PRO4404	breast tumor	universal normal control
	PRO4404	rectal tumor	universal normal control
	PRO1884	lung tumor	universal normal control
	PRO4349	colon tumor	universal normal control
55	PRO4349	lung tumor	universal normal control

		Table 8 (cont')	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO4401	colon tumor	universal normal control
	PRO4401	lung tumor	universal normal control
	PRO1867	lung tumor	universal normal control
5	PRO1867	liver tumor	universal normal control
	PRO4319	breast tumor	universal normal control
	PRO4319	lung tumor	universal normal control
	PRO4991	lung tumor	universal normal control
	PRO4991	colon tumor	universal normal control
10	PRO4398	lung tumor	universal normal control
~~	PRO4346	lung tumor	universal normal control
	PRO4350	colon tumor	universal normal control
	PRO4350	prostate tumor	universal normal control
	PRO4350		universal normal control
15	PRO4318	lung tumor	universal normal control
13	PRO4318	prostate tumor	universal normal control
	PRO4318 PRO4340	lung tumor	universal normal control
		breast tumor	universal normal control
	PRO4340	lung tumor	universal normal control
20	PRO4400	breast tumor	
20	PRO4400	lung tumor	universal normal control
	PRO4320	lung tumor	universal normal control
	PRO4409	lung tumor	universal normal control
	PRO4409	cervical tumor	universal normal control
25	PRO4409	colon tumor	universal normal control
25	PRO4399	lung tumor	universal normal control
	PRO4399	breast tumor	universal normal control
	PRO4418	lung tumor	universal normal control
	PRO4418	breast tumor	universal normal control
20	PRO4330	cervical tumor	universal normal control
30	PRO4330	colon tumor	matched normal colon control
	PRO4339	breast tumor	universal normal control
	PRO4339	colon tumor	universal normal control
	PRO4326	lung tumor	universal normal control
	PRO4326	colon tumor	universal normal control
35	PRO6014	breast tumor	universal normal control
	PRO3446	colon tumor	universal normal control
	PRO3446	lung tumor	universal normal control
	PRO4322	lung tumor	universal normal control
40	PRO4322	rectal tumor	universal normal control
40	PRO4322	colon tumor	matched normal colon control
	PRO4381	breast tumor	universal normal control
	PRO4381	lung tumor	universal normal control
	PRO4381	colon tumor	universal normal control
	PRO4348	lung tumor	universal normal control
45	PRO4348	prostate tumor	universal normal control
	PRO4371	breast tumor	universal normal control
	PRO3742	colon tumor	universal normal control
	PRO3742	lung tumor	universal normal control
	PRO5773	lung tumor	universal normal control
50	PRO5773	colon tumor	universal normal control
	PRO5773	prostate tumor	universal normal control
	PRO5774	colon tumor	universal normal control
	PRO4343	colon tumor	universal normal control
	PRO4325	lung tumor	universal normal control
55	PRO4347	lung tumor	universal normal control
		•	

		Table o (cont.)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO4347	colon tumor	universal normal control
	PRO4347	rectal tumor	universal normal control
	PRO3743	colon tumor	universal normal control
5	PRO3743	lung tumor	universal normal control
	PRO3743	prostate tumor	universal normal control
	PRO4426	colon tumor	universal normal control
	PRO4500	colon tumor	universal normal control
	PRO4389	breast tumor	universal normal control
10	PRO4389	lung tumor	universal normal control
	PRO4337	colon tumor	universal normal control
	PRO4337	breast tumor	universal normal control
	PRO4337	lung tumor	universal normal control
	PRO4992	lung tumor	universal normal control
15	PRO5996	lung tumor	universal normal control
	PRO4345	lung tumor	universal normal control
	PRO4345	colon tumor	universal normal control
	PRO5780	lung tumor	universal normal control
	PRO5780	breast tumor	universal normal control
20	PRO5992	lung tumor	universal normal control
	PRO5992	colon tumor	universal normal control
	PRO5992	breast tumor	universal normal control
	PRO4428	prostate tumor	universal normal control
	PRO4994	lung tumor	universal normal control
25	PRO5995	lung tumor	universal normal control
	PRO5995	colon tumor	universal normal control
	PRO6094	lung tumor	universal normal control
	PRO6094	colon tumor	universal normal control
	PRO4317	lung tumor	universal normal control
30	PRO4317	colon tumor	universal normal control
	PRO4317	liver tumor	universal normal control
	PRO4317	colon tumor	matched normal colon control
	PRO5997	colon tumor	universal normal control
	PRO5997	lung tumor	universal normal control
35	PRO5005	lung tumor	universal normal control
	PRO5005	colon tumor	universal normal control
	PRO5004	colon tumor	universal normal control
	PRO6001	breast tumor	universal normal control
	PRO6013	colon tumor	universal normal control
40	PRO4502	lung tumor	universal normal control
	PRO4502	colon tumor	universal normal control
	PRO6007	breast tumor	universal normal control
	PRO6028	breast tumor	universal normal control
	PRO6028	colon tumor	universal normal control
45	PRO4327	prostate tumor	universal normal control
	PRO4315	colon tumor	universal normal control
	PRO5993	lung tumor	universal normal control
	PRO5993	colon tumor	universal normal control
	PRO4503	colon tumor	universal normal control
50	PRO4976	lung tumor	universal normal control
	PRO5798	lung tumor	universal normal control
	PRO5798	colon tumor	universal normal control
	PRO6242	colon tumor	universal normal control
	PRO6242	colon tumor	matched normal colon control
55	PRO6242	breast tumor	universal normal control
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		Table 8 (cont')	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO6242	liver tumor	universal normal control
	PRO6242	rectal tumor	universal normal control
	PRO6095	breast tumor	universal normal control
5	PRO6095	lung tumor	universal normal control
	PRO6093	colon tumor	universal normal control
	PRO6093	breast tumor	universal normal control
	PRO6093	lung tumor	universal normal control
	PRO6093	colon tumor	matched normal colon control
10	PRO6012	colon tumor	universal normal control
10	PRO6027	*****	universal normal control
	PRO6027	lung tumor colon tumor	universal normal control
	PRO6027	rectal tumor	universal normal control
	PRO6181		universal normal control
15		prostate tumor	universal normal control
13	PRO6181	lung tumor	universal normal control
	PRO6181	colon tumor	
	PRO6097	colon tumor	universal normal control
	PRO6097	lung tumor	universal normal control
20	PRO6090	lung tumor	universal normal control
20 .	PRO7171	lung tumor	universal normal control
	PRO7171	colon tumor	universal normal control
	PRO7171	breast tumor	universal normal control
	PRO6258	prostate tumor	universal normal control
05	PRO6258	breast tumor	universal normal control
25	PRO6258	cervical tumor	universal normal control
	PRO6258	liver tumor	universal normal control
	PRO6258	colon tumor	universal normal control
	PRO9820	prostate tumor	universal normal control
••	PRO6243	lung tumor	universal normal control
30	PRO6182	lung tumor	universal normal control
	PRO6079	lung tumor	universal normal control
	PRO6079	colon tumor	universal normal control
	PRO6079	breast tumor	universal normal control
	PRO6079	prostate tumor	universal normal control
35	PRO7434	lung tumor	universal normal control
	PRO9865	colon tumor	universal normal control
	PRO9828	colon tumor	universal normal control
	PRO196	colon tumor	universal normal control
	PRO196	lung tumor	universal normal control
40	PRO196	breast tumor	universal normal control
	PRO197	colon tumor	universal normal control
	PRO197	lung tumor	universal normal control
	PRO197	breast tumor	universal normal control
	PRO195	colon tumor	universal normal control
45	PRO195	lung tumor	universal normal control
	PRO195	breast tumor	universal normal control
	PRO187	lung tumor	universal normal control
	PRO187	liver tumor	universal normal control
	PRO182	colon tumor	universal normal control
50	PRO182	lung tumor	universal normal control
	PRO182	breast tumor	universal normal control
	PRO188	rectal tumor	universal normal control
	PRO183	colon tumor	universal normal control
	PRO183	lung tumor	universal normal control
55	PRO183	breast tumor	universal normal control

	•	Table 6 (cont)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO183	rectal tumor	universal normal control
	PRO184	lung tumor	universal normal control
_	PRO184	breast tumor	universal normal control
5	PRO185	lung tumor	universal normal control
	PRO200	colon tumor	universal normal control
	PRO200	lung tumor	universal normal control
	PRO200	breast tumor	universal normal control
	PRO200	rectal tumor	universal normal control
10	PRO202	colon tumor	universal normal control
	PRO202	lung tumor	universal normal control
	PRO202	breast tumor	universal normal control
	PRO202	rectal tumor	universal normal control
	PRO202	liver tumor	universal normal control
15	PRO214	colon tumor	universal normal control
	PRO214	lung tumor	universal normal control
	PRO215	colon tumor	universal normal control
	PRO215	lung tumor	universal normal control
•	PRO215	breast tumor	universal normal control
20	PRO219	colon tumor	universal normal control
	PRO219	lung tumor	universal normal control
	PRO219	breast tumor	universal normal control
	PRO219	liver tumor	universal normal control
	PRO211	lung tumor	universal normal control
25	PRO211	breast tumor	universal normal control
	PRO220	colon tumor	universal normal control
	PRO220	lung tumor	universal normal control
	PRO220	breast tumor	universal normal control
	PRO366	colon tumor	universal normal control
30	PRO366	lung tumor	universal normal control
	PRO366	breast tumor	universal normal control
	PRO216	lung tumor	universal normal control
	PRO221	colon tumor	universal normal control
	PRO221	lung tumor	universal normal control
35	PRO221	breast tumor	universal normal control
	PRO228	lung tumor	universal normal control
	PRO228	breast tumor	universal normal control
	PRO217	lung tumor	universal normal control
	PRO217	breast tumor	universal normal control
40	PRO222	colon tumor	universal normal control
	PRO222	lung tumor	universal normal control
	PRO222	breast tumor	universal normal control
	PRO224	colon tumor	universal normal control
	PRO224	lung tumor	universal normal control
45	PRO224	breast tumor	universal normal control
	PRO224	prostate tumor	universal normal control
	PRO224	rectal tumor	universal normal control
	PRO230	colon tumor	universal normal control
	PRO230	lung tumor	universal normal control
50	PRO230	breast tumor	universal normal control
	PRO230	prostate tumor	universal normal control
	PRO198	colon tumor	universal normal control
	PRO198	lung tumor	universal normal control
	PRO198	breast tumor	universal normal control
55	PRO198	liver tumor	universal normal control
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		Table 8 (cont.)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO226	lung tumor	universal normal control
	PRO226	breast tumor	universal normal control
	PRO261	lung tumor	universal normal control
5	PRO242	colon tumor	universal normal control
	PRO242	lung tumor	universal normal control
	PRO242	breast tumor	universal normal control
	PRO227	colon tumor	universal normal control
	PRO227	lung tumor	universal normal control
10	PRO237	colon tumor	universal normal control
	PRO237	lung tumor	universal normal control
•	PRO237	breast tumor	universal normal control
	PRO237	prostate tumor	universal normal control
	PRO241	colon tumor	universal normal control
15	PRO241	lung tumor	universal normal control
	PRO241	breast tumor	universal normal control
	PRO231	colon tumor	universal normal control
	PRO231	lung tumor	universal normal control
	PRO231	breast tumor	universal normal control
20	PRO231	rectal tumor	universal normal control
20	PRO235	colon tumor	universal normal control
	PRO235	lung tumor	universal normal control
	PRO235	breast tumor	universal normal control
	PRO235	liver tumor	universal normal control
25	PRO323	lung tumor	universal normal control
	PRO323	breast tumor	universal normal control
	PRO323	rectal tumor	universal normal control
	PRO245	colon tumor	universal normal control
	PRO245	lung tumor	universal normal control
30	PRO245	breast tumor	universal normal control
	PRO245	cervical tumor	universal normal control
	PRO245	liver tumor	universal normal control
	PRO246	colon tumor	universal normal control
	PRO246	lung tumor	universal normal control
35	PRO246	breast tumor	universal normal control
	PRO288	lung tumor	universal normal control
	PRO288	breast tumor	universal normal control
	PRO248	lung tumor	universal normal control
	PRO248	rectal tumor	universal normal control
40	PRO257	colon tumor	universal normal control
	PRO257	lung tumor	universal normal control
	PRO257	prostate tumor	universal normal control
	PRO172	colon tumor	universal normal control
	PRO172	lung tumor	universal normal control
45	PRO172	breast tumor	universal normal control
1.5	PRO258	colon tumor	universal normal control
	PRO258	lung tumor	universal normal control
	PRO258	breast tumor	universal normal control
	PRO265	lung tumor	universal normal control
50	PRO265	breast tumor	universal normal control
50	PRO265	rectal tumor	universal normal control
	PRO326	colon tumor	universal normal control
	PRO326	lung tumor	universal normal control
55	PRO326	breast tumor	universal normal control
<i>JJ</i>	PRO326	liver tumor	universal normal control

		Table 8 (cont.)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO266	colon tumor	universal normal control
	PRO266	lung tumor	universal normal control
	PRO266	breast tumor	universal normal control
5	PRO269	lung tumor	universal normal control
	PRO269	rectal tumor	universal normal control
	PRO285	colon tumor	universal normal control
	PRO285	lung tumor	universal normal control
	PRO285	breast tumor	universal normal control
10	PRO328	colon tumor	universal normal control
	PRO328	lung tumor	universal normal control
	PRO328	breast tumor	universal normal control
	PRO344	breast tumor	universal normal control
	PRO272	lung tumor	universal normal control
15	PRO301	colon tumor	universal normal control
	PRO301	lung tumor	universal normal control
	PRO301	breast tumor	universal normal control
	PRO331	colon tumor	universal normal control
	PRO331	lung tumor	universal normal control
20	PRO331	breast tumor	universal normal control
	PRO332	colon tumor	universal normal control
	PRO332	lung tumor	universal normal control
	PRO332	breast tumor	universal normal control
	PRO353	colon tumor	universal normal control
25	PRO353	lung tumor	universal normal control
	PRO353	breast tumor	universal normal control
	PRO310	colon tumor	universal normal control
	PRO310	lung tumor	universal normal control
	PRO310	breast tumor	universal normal control
30	PRO310	rectal tumor	universal normal control
	PRO337	colon tumor	universal normal control
	PRO337	lung tumor	universal normal control
	PRO337	breast tumor	universal normal control
	PRO346	lung tumor	universal normal control
35 .	PRO350	lung tumor	universal normal control
	PRO350	breast tumor	universal normal control
	PRO526	colon tumor	universal normal control
	PRO526	lung tumor	universal normal control
40	PRO526	breast tumor	universal normal control
40	PRO381	colon tumor	universal normal control
	PRO381	lung tumor	universal normal control
	PRO381	breast tumor	universal normal control
	PRO381	prostate tumor	universal normal control
45	PRO846	colon tumor	universal normal control
45	PRO846	lung tumor	universal normal control
	PRO363	colon tumor	universal normal control
	PRO363	lung tumor	universal normal control
	PRO365	lung tumor	universal normal control
50	PRO365	breast tumor	universal normal control
50	PRO1310	breast tumor	universal normal control
	PRO731 PRO731	colon tumor	universal normal control
	-	lung tumor	universal normal control
	PRO731	breast tumor	universal normal control
55	PRO322	colon tumor	universal normal control
JJ	PRO322	lung tumor	umversar normai control

		<u>lable 8 (cont.)</u>	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO322	breast tumor	universal normal control
	PRO322	rectal tumor	universal normal control
	PRO322	liver tumor	universal normal control
5	PRO536	lung tumor	universal normal control
-	PRO536	breast tumor	universal normal control
	PRO536	liver tumor	universal normal control
	PRO719	colon tumor	universal normal control
	PRO719	lung tumor	universal normal control
10	PRO719	breast tumor	universal normal control
10	PRO619	colon tumor	universal normal control
	PRO619		universal normal control
	PRO619	lung tumor	universal normal control
		breast tumor	universal normal control
15	PRO771	colon tumor	universal normal control
13	PRO771	lung tumor	universal normal control
	PRO771	breast tumor	
	PRO1083	colon tumor	universal normal control
	PRO1083	lung tumor	universal normal control
20	PRO1083	breast tumor	universal normal control
20	PRO1083	prostate tumor	universal normal control
	PRO862	colon tumor	universal normal control
	PRO862	lung tumor	universal normal control
	PRO862	breast tumor	universal normal control
0.5	PRO733	colon tumor	universal normal control
25	PRO733	lung tumor	universal normal control
	PRO733	breast tumor	universal normal control
	PRO733	liver tumor	universal normal control
	PRO1188	lung tumor	universal normal control
	PRO1188	breast tumor	universal normal control
30	PRO1188	rectal tumor	universal normal control
	PRO770	lung tumor	universal normal control
	PRO770	breast tumor	universal normal control
	PRO1080	colon tumor	universal normal control
	PRO1080	lung tumor	universal normal control
35	PRO1080	breast tumor	universal normal control
	PRO1017	colon tumor	universal normal control
	PRO1017	lung tumor	universal normal control
	PRO1017	breast tumor	universal normal control
	PRO1016	colon tumor	universal normal control
40	PRO1016	lung tumor	universal normal control
	PRO1016	breast tumor	universal normal control
	PRO1016	rectal tumor	universal normal control
	PRO792	lung tumor	universal normal control
	PRO938	colon tumor	universal normal control
45	PRO938	lung tumor	universal normal control
	PRO938	breast tumor	universal normal control
	PRO1012	colon tumor	universal normal control
	PRO1012	lung tumor	universal normal control
	PRO1012	rectal tumor	universal normal control
50	PRO1012	liver tumor	universal normal control
	PRO1008	lung tumor	universal normal control
	PRO1075	colon tumor	universal normal control
	PRO1075	lung tumor	universal normal control
	PRO1007	colon tumor	universal normal control
55	PRO1007	lung tumor	universal normal control

		Table 6 (cont)	_
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO1007	breast tumor	universal normal control
	PRO1007	rectal tumor	universal normal control
	PRO1056	colon tumor	universal normal control
5	PRO1056	lung tumor	universal normal control
	PRO1056	breast tumor	universal normal control
	PRO791	colon tumor	universal normal control
	PRO791	lung tumor	universal normal control
	PRO791	breast tumor	universal normal control
10	PRO791	rectal tumor	universal normal control
	PRO1111	colon tumor	universal normal control
	PRO1111	lung tumor	universal normal control
	PRO1111	breast tumor	universal normal control
	PRO812	lung tumor	universal normal control
15	PRO812	breast tumor	universal normal control
	PRO812	rectal tumor	universal normal control
	PRO1066	lung tumor	universal normal control
	PRO1185	colon tumor	universal normal control
	PRO1185	lung tumor	universal normal control
20	PRO1185	breast tumor	universal normal control
	PRO1031	lung tumor	universal normal control
	PRO1360	lung tumor	universal normal control
	PRO1360	breast tumor	universal normal control
	PRO1309	lung tumor	universal normal control
25	PRO1309	breast tumor	universal normal control
	PRO1107	lung tumor	universal normal control
	PRO1107	breast tumor	universal normal control
	PRO836	colon tumor	universal normal control
	PRO836	lung tumor	universal normal control
30	PRO1132	lung tumor	universal normal control
	PRO1132	breast tumor	universal normal control
	PRO1131	colon tumor	universal normal control
	PRO1131	lung tumor	universal normal control
	. PRO1131	breast tumor	universal normal control
35	PRO1131	liver tumor	universal normal control
	PRO1130	colon tumor	universal normal control
	PRO1130	lung tumor	universal normal control
	PRO1130	breast tumor	universal normal control
	PRO844	colon tumor	universal normal control
40	PRO844	lung tumor	universal normal control
	PRO844	breast tumor	universal normal control
•	PRO844	rectal tumor	universal normal control
	PRO1154	colon tumor	universal normal control
	PRO1154	lung tumor	universal normal control
45	PRO1154	rectal tumor	universal normal control
	PRO1154	liver tumor	universal normal control
	PRO1181	lung tumor	universal normal control
	PRO1181	breast tumor	universal normal control
	PRO1126	colon tumor	universal normal control
50	PRO1126	lung tumor	universal normal control
	PRO1126	breast tumor	universal normal control
	PRO1126	adrenal tumor	universal normal control
	PRO1186	colon tumor	universal normal control
	PRO1186	lung tumor	universal normal control
55	PRO1186	breast tumor	universal normal control

		Table 8 (cont.)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO1186	liver tumor	universal normal control
	PRO1198	colon tumor	universal normal control
_	PRO1198	lung tumor	universal normal control
5	PRO1159	lung tumor	universal normal control
	PRO1159	breast tumor	universal normal control
	PRO1159	liver tumor	universal normal control
	PRO1265	colon tumor	universal normal control
	PRO1265	breast tumor	universal normal control
10	PRO1250	colon tumor	universal normal control
	PRO1250	lung tumor	universal normal control
	PRO1250	breast tumor	universal normal control
	PRO1475	colon tumor	universal normal control
	PRO1475	breast tumor	universal normal control
15	PRO1312	colon tumor	universal normal control
	PRO1312	lung tumor	universal normal control
	PRO1312	breast tumor	universal normal control
	PRO1308	colon tumor	universal normal control
20	PRO1308	lung tumor	universal normal control
20	PRO1308	liver tumor	universal normal control
	PRO1326	colon tumor	universal normal control
	PRO1325	lung tumor	universal normal control
	PRO1326	breast tumor	universal normal control
25	PRO1192	colon tumor	universal normal control
25	PRO1192	lung tumor	universal normal control
	PRO1192	breast tumor	universal normal control
	PRO1246	colon tumor	universal normal control
	PRO1246	lung tumor	universal normal control
30	PRO1246	breast tumor	universal normal control
30	PRO1246	prostate tumor	universal normal control
	PRO1356 PRO1356	colon tumor	universal normal control
	PRO1356	lung tumor	universal normal control
	PRO1275	breast tumor.	universal normal control
35	PRO1275	lung tumor breast tumor	universal normal control
33	PRO1274	lung tumor	universal normal control
	PRO1358	colon tumor	universal normal control
	PRO1358	lung tumor	universal normal control
	PRO1358	prostate tumor	universal normal control
40	PRO1286	colon tumor	universal normal control
. •	PRO1286	lung tumor	universal normal control
	PRO1286	prostate tumor	universal normal control
	PRO1286	rectal tumor	universal normal control
	PRO1294	colon tumor	universal normal control
45	PRO1294	lung tumor	universal normal control
	PRO1294	breast tumor	universal normal control
	PRO1294	rectal tumor	universal normal control
	PRO1273	lung tumor	universal normal control
	PRO1273	rectal tumor	universal normal control
50	PRO1279	colon tumor	universal normal control
	PRO1279	lung tumor	universal normal control
	PRO1195	lung tumor	universal normal control
	PRO1195	breast tumor	universal normal control
	PRO1271	lung tumor	universal normal control
55	PRO1271	breast tumor	universal normal control

		Table 8 (Coll)	
	<u>Molecule</u>	is overexpressed in:	as compared to:
-		liver tumor	universal normal control
		colon tumor	universal normal control
_		lung tumor	universal normal control
5	PRO1338	breast tumor	universal normal control
•	PRO1343	colon tumor	universal normal control
	PRO1343	lung tumor	universal normal control
		breast tumor	universal normal control
		rectal tumor	universal normal control
10		lung tumor	universal normal control
	PRO1418	lung tumor	universal normal control
	PRO1418	liver tumor	universal normal control
		colon tumor	universal normal control
	PRO1387	lung tumor	universal normal control
15	PRO1387	prostate tumor	universal normal control
	PRO1387	rectal tumor	universal normal control
		colon tumor	universal normal control
		lung tumor	universal normal control
•		colon tumor	universal normal control
20		lung tumor	universal normal control
		prostate tumor	universal normal control
		colon tumor	universal normal control
		lung tumor	universal normal control
0.5		breast tumor	universal normal control
25		rectal tumor	universal normal control
		colon tumor	universal normal control
		lung tumor	universal normal control
	PRO1271 liver PRO1338 color PRO1338 lung PRO1338 breaz PRO1343 color PRO1343 lung PRO1343 breaz PRO1344 lung PRO1444 lung PRO1418 liver PRO1387 prost PRO1387 prost PRO1384 color PRO1384 lung PRO1384 lung PRO1384 lung PRO1565 color PRO1565 lung PRO1565 prost PRO1474 lung PRO1474 precta PRO1474 precta PRO1917 color PRO1917 lung PRO1917 breas PRO1787 color PRO1787 lung PRO1787 lung PRO1787 lung PRO1787 breas PRO1566 breas PRO1566 lung PRO1566 prost PRO1566 lung PRO1566 prost PRO1566 lung PRO1566 prost PRO1566 lung PRO1566 precta	breast tumor	universal normal control
20		colon tumor	universal normal control
30		lung tumor	universal normal control
		breast tumor	universal normal control
		lung tumor	universal normal control
		breast tumor	universal normal control
25		colon tumor	universal normal control
35		lung tumor	universal normal control
		rectal tumor	universal normal control
		colon tumor	universal normal control
		lung tumor	universal normal control
40		breast tumor	universal normal control
70		lung tumor	
		breast tumor	universal normal control
		colon tumor	universal normal control universal normal control
	·	lung tumor	universal normal control
45		breast tumor	universal normal control
43		prostate tumor	universal normal control
		colon tumor	universal normal control
		breast tumor	universal normal control
		lung tumor breast tumor	universal normal control
50			•
<i>5</i> 0		colon tumor	universal normal control universal normal control
		lung tumor	universal normal control
		lung tumor	universal normal control
		breast tumor	
		colon tumor	universal normal control universal normal control
<i></i>	1 1107302	lung tumor	minacisar morniar control

Table 8 (cont')

	<u>Molecule</u>	is overexpressed in:	as compared to:
	PRO4302	breast tumor	universal normal control
	PRO4302	prostate tumor	universal normal control
_	PRO5990	colon tumor	universal normal control
	PRO5990	lung tumor	universal normal control
	PRO5990	breast tumor	universal normal control

EXAMPLE 31: Identification of Receptor/Ligand Interactions

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In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor or ligand molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparaion of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin). Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (e.g. Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (e.g. FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have

been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

Using these assays, the following receptor/ligand interactions have been herein identified:

- (1) PRO1801 binds to PRO1114 and PRO4978.
- (2) PRO100 binds to PRO1114.

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The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

PCT P3330R1 Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM Form - PCT/RO/134 (EASY) Indications Relating to Deposited Microorganism(s) or Other Biological Material (PCT Rule 13bis) 0-1-1 Prepared using PCT-EASY Version 2.91 (updated 10.10.2000) 0-2 International Application No. 0-3 Applicant's or agent's file reference P3330R1 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 1-1 page 98 1-2 line 34 1-3 Identification of Deposit 1-3-1 Name of depositary institution American Type Culture Collection 1-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 1-3-3 Date of deposit 14 April 1998 (14.04.1998) 1-3-4 Accession Number ATCC 209771 1-4 Additional Indications NONE 1-5 **Designated States for Which** all designated States Indications are Made 1-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 2 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 2-1 page 98 2-2 35 2-3 **Identification of Deposit** 2-3-1 Name of depositary institution American Type Culture Collection 2-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 2-3-3 Date of deposit 09 February 1999 (09.02.1999) 2-3-4 **Accession Number** ATCC 203654 Additional Indications 2-4 NONE 2-5 **Designated States for Which** all designated States Indications are Made 2-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 3-1 page

98

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3-2

line

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3-3	Identification of Deposit	
3-3-1	Name of depositary institution	American Type Culture Collection
3-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
3-3-3	Date of deposit	25 May 1999 (25.05.1999)
3-3-4	Accession Number	ATCC PTA-127
3-4	Additional Indications	NONE
3-5	Designated States for Which	all designated States
3-6	Indications are Made	
3-0	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
4	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
4-1	page	98
4-2	line	37
4-3 4-3-1	Identification of Deposit Name of depositary institution	
4-3-1	· · · ·	American Type Culture Collection
4-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
4-3-3	Date of deposit	America
4-3-4	Accession Number	27 July 1999 (27.07.1999)
4-3-4	Additional Indications	ATCC PTA-429
4-5	Designated States for Which	NONE
4-5	Indications are Made	all designated States
4-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
5	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
5-1	page	98
5-2	line	38
5-3	Identification of Deposit	
5-3-1	Name of depositary institution	American Type Culture Collection
5-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
5-3-3	Date of deposit	27 July 1999 (27.07.1999)
5-3-4	A 1 11/4 T 15 15 15 15 15 15 15 15 15 15 15 15 15	ATCC PTA-432
5-4		NONE
5-5	Designated States for Which Indications are Made	all designated States
5-6	<u> </u>	NONE
	These indications will be submitted to	
	the International Bureau later	

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6	The indications made below relate to the deposited microorganism(s) or other biological material materials.	
	other biological material referred to in the description on:	1
6-1 -	page	98
6-2	line	39
6-3	Identification of Deposit	
6-3-1	Name of depositary institution	American Type Culture Collection
6-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
6-3- 3	Date of deposit	10 December 1997 (10.12.1997)
6-3-4	Accession Number	ATCC 209525
6-4	Additional Indications	NONE
6-5	Designated States for Which	all designated States
6-6	Indications are Made Separate Furnishing of Indications	
	These indications will be submitted to	NONE
	the International Bureau later	
7	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
7-1	page	99
7-2	line	[2
7-3 7-3-1	Identification of Deposit	
7-3-1	Name of depositary institution	American Type Culture Collection
7-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
7-3-3	Data of densell	America
7-3-3 7-3-4	Date of deposit	12 January 1999 (12.01.1999)
7-3-4	Accession Number	ATCC 203577
7-5	Additional Indications	NONE
7-5	Designated States for Which Indications are Made	all designated States
7-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
8	the International Bureau later	
0	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
8-1	the description on: page	00
8-2	i. •	99
8-3	Identification of Deposit	3
8-3-1	Ma (A 1) 11 11	American Type Culture Collection
8-3-2	laga a.s. n	10801 University Blvd., Manassas,
	• • • • • • • • • • • • • • • • • • • •	Virginia 20110-2209United States of
		virginia 20110-22090nited States of America
8-3-3		
8-3-4		27 July 1999 (27.07.1999)
8-4	A Julia 1 L. di 1	ATCC PTA-430
8-5	D	NONE
- 1	Indications are Made	all designated States

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8-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
9	the International Bureau later The indications made below relate to	
•	the deposited microorganism(s) or	
	other biological material referred to in	
9-1	the description on:	
9-2	line	99
9-3	Identification of Deposit	4
9-3-1	Name of depositary institution	Amenican Mome Culture Callection
9-3-2	Address of depositary institution	American Type Culture Collection
	Transfer of depositary motivation	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
9-3-3	Date of deposit	America
9-3-4	•	08 June 1999 (08.06.1999)
9-3-4	Accession Number	ATCC PTA-203
	Additional Indications	NONE
9-5	Designated States for Which Indications are Made	all designated States
9-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
10	the International Bureau later	
10	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
10-1	page	99
10-2	line	5
10-3	Identification of Deposit	
10-3-1	Name of depositary institution	American Type Culture Collection
10-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
10-3-3	Date of deposit	01 July 1998 (01.07.1998)
10-3-4	Accession Number	ATCC 203040
10-4	Additional Indications	NONE
10-5	Designated States for Which	all designated States
10-6	Indications are Made	
10-0	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
11	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
11-1	page	99
11-2	line	6
11-3	Identification of Deposit	
11-3-1	1	American Type Culture Collection
11-3-2		10801 University Blvd., Manassas,
	1	Virginia 20110-2209United States of
	l l	America
11-3-3	margin 1	
11-3-4		31 August 1999 (31.08.1999)
		ATCC PTA-611

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11-4	Additional Indications	NONE
11-5	Designated States for Which Indications are Made	all designated States
11-6	Separate Furnishing of Indications	NONE
_	These indications will be submitted to the International Bureau later	
12	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
12-1	page	99
12-2	line	7
12-3	Identification of Deposit	
12-3-1	Name of depositary institution	American Type Culture Collection
12-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
12-3-3	Date of deposit	21 January 1998 (21.01.1998)
12-3-4	Accession Number	ATCC 209593
12-4	Additional Indications	NONE
12-5	Designated States for Which Indications are Made	all designated States
12-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
13	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
13-1	page	99
13-2	line	8
13-3	Identification of Deposit	
13-3-1	Name of depositary institution	American Type Culture Collection
13-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
13-3-3	Date of deposit	09 February 1999 (09.02.1999)
13-3-4	Accession Number	ATCC 203649
13-4	Additional Indications	NONE
13-5	Designated States for Which Indications are Made	all designated States
13-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
14	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
14-1	page	99
14-2	line	9

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14-3	Identification of Deposit	
14-3-1	Name of depositary institution	American Type Culture Collection
14-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
14-3-3	Date of deposit	12 January 1999 (12.01.1999)
14-3-4	Accession Number	ATCC 203574
14-4	Additional Indications	NONE
14-5	Designated States for Which	all designated States
44.5	Indications are Made	all designated states
14-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
15	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
15-1	page	99
15-2	line	10
15-3	Identification of Deposit	
15-3-1	Name of depositary institution	American Type Culture Collection
15-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
45.2.2	Data of damage	America
15-3-3	Date of deposit	25 May 1999 (25.05.1999)
15-3-4	Accession Number	ATCC PTA-129
15-4	Additional Indications	NONE
15-5	Designated States for Which Indications are Made	all designated States
15-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
16	the International Bureau later The Indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
16-1	page	99
16-2	line	11
16-3	Identification of Deposit	
16-3-1	Name of depositary institution	American Type Culture Collection
16-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
16-3-3	Date of deposit	27 May 1998 (27.05.1998)
16-3-4		ATCC 209905
16-4	Additional Indications	NONE
16-5	Designated States for Which Indications are Made	all designated States
16-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	

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17	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
17-1	page	99
17-2	line	12
17-3	Identification of Deposit	
17-3-1	Name of depositary institution	American Type Culture Collection
17-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
47.00		America
17-3-3	Date of deposit	12 January 1999 (12.01.1999)
17-3-4	Accession Number	ATCC 203585
17-4	Additional Indications	NONE
17-5	Designated States for Which Indications are Made	all designated States
17-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
18	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
18-1	page	99
18-2	line	13
18-3	Identification of Deposit	
18-3-1	Name of depositary institution	American Type Culture Collection
18-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
18-3-3	Date of deposit	09 February 1999 (09.02.1999)
18-3-4	Accession Number	ATCC 203665
18-4	Additional Indications	NONE
18-5	Designated States for Which Indications are Made	all designated States
18-6	Separate Furnishing of Indications	NONE
a.	These indications will be submitted to	
19	the International Bureau later	
13	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
19-1	page	99
19-2	line	14
19-3	Identification of Deposit	
19-3-1	Name of depositary institution	American Type Culture Collection
19-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
19-3-3	Date of deposit	27 July 1999 (27.07.1999)
19-3-4	Accession Number	ATCC PTA-427
19-4		NONE
19-5	Designated States for Which Indications are Made	all designated States

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19-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
20	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
20-1	page	99
20-2	line	15
20-3	Identification of Deposit	
20-3-1	Name of depositary institution	American Type Culture Collection
20-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
20-3-3	Date of deposit	31 August 1999 (31.08.1999)
20-3-4	Accession Number	ATCC PTA-615
20-4	Additional Indications	NONE
20-5	Designated States for Which Indications are Made	all designated States
20-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
21	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
21-1	page	99
21-2	line	16
21-3 21-3-1	Identification of Deposit	
21-3-1	Name of depositary institution	American Type Culture Collection
21-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
21-3-3	Date of descrip	America
21-3-3	Date of deposit	12 January 1999 (12.01.1999)
	Accession Number	ATCC 203582
21-4	Additional Indications	NONE
21-5	Designated States for Which Indications are Made	all designated States
21-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
22	the International Bureau later	
44	The indications made below relate to the deposited microorganism(s) or	•
	other biological material referred to in	
22-1	the description on:	
22-1	line	99
22-2	Identification of Deposit	17
22-3 22-3-1	Name of depositary institution	Amoriana Mumo Culture Collection
22-3-2	Address of depositary institution	American Type Culture Collection
•		10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
22-3-3	Date of deposit	America
22-3-3 22-3-4	Accession Number	09 March 1999 (09.03.1999)
	Accession Number	ATCC 203838

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22-4	Additional Indications	NONE
22-5	Designated States for Which Indications are Made	all designated States
22-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
23	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
23-1	the description on:	99
23-2	line	18
23-3	Identification of Deposit	
23-3-1	Name of depositary institution	American Type Culture Collection
23-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
23-3-3	Date of deposit	27 July 1999 (27.07.1999)
23-3-4	Accession Number	ATCC PTA-428
23-4	Additional Indications	NONE
23-5	Designated States for Which Indications are Made	all designated States
23-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
24	The indications made below relate to the deposited microorganism(s) or other biological material referred to in	
	the description on:	
24-1	the description on:	99
24-1 24-2	the description on:	
24-2 24-3	the description on: page line Identification of Deposit	99
24-2 24-3 24-3-1	the description on: page line	99
24-2 24-3	the description on: page line Identification of Deposit	99 19
24-2 24-3 24-3-1	the description on: page line Identification of Deposit Name of depositary institution	99 19 American Type Culture Collection
24-2 24-3 24-3-1 24-3-2	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution	99 19 American Type Culture Collection 10801 University Blvd., Manassas,
24-2 24-3 24-3-1 24-3-2 24-3-3	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999)
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4 24-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836 NONE
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4 24-4 24-5	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836 NONE all designated States
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4 24-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836 NONE all designated States
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4 24-4 24-5	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in	99 19 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836 NONE all designated States
24-2 24-3 24-3-1 24-3-2 24-3-3 24-3-4 24-4 24-5 24-6	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other blological material referred to in the description on:	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 March 1999 (09.03.1999) ATCC 203836 NONE all designated States NONE

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25-3	Identification of Denseit	
25-3 25-3-1	Identification of Deposit Name of depositary institution	Promison Three Cultures Callaghian
25-3-2	Address of depositary institution	American Type Culture Collection
20-0-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
25.2.2	But of delivery	America
25-3-3	Date of deposit	08 June 1999 (08.06.1999)
25-3-4	Accession Number	ATCC PTA-205
25-4	Additional Indications	NONE
25-5	Designated States for Which Indications are Made	all designated States
25-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
26	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
26-1	page	 99
26-2	line	21
26-3	Identification of Deposit	21
26-3-1	Name of depositary institution	American Type Culture Collection
26-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		, · · · · · · · · · · · · · · · · · · ·
		Virginia 20110-2209United States of America
26-3-3	Date of deposit	
26-3-4	Accession Number	27 July 1999 (27.07.1999) ATCC PTA-431
26-4	Additional Indications	
26-5	Designated States for Which	NONE
	Indications are Made	all designated States
26-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
27	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	,
	the description on:	
27-1	page	99
27-2	line	22
27-3 27-3-1	Identification of Deposit Name of depositary institution	
	_	American Type Culture Collection
21-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
07.00	Data of damas's	America
27-3-3	Date of deposit	09 February 1999 (09.02.1999)
27-3-4	Accession Number	ATCC 203659
27-4	Additional Indications	NONE
27-5	Designated States for Which	all designated States
27-5 27-6	Indications are Made	
	Indications are Made	all designated States NONE

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28	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in	
28-1	the description on:	00
28-2	line	99
28-3	Identification of Deposit	23
28-3-1	Name of depositary institution	American Type Culture Collection
28-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
28-3-3	Date of deposit	12 January 1999 (12.01.1999)
28-3-4	Accession Number	ATCC 203584
28-4	Additional Indications	
28-5	Designated States for Which	NONE
20-3	Indications are Made	all designated States
28-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
29	the International Bureau later The indications made below relate to	
23	the deposited microorganism(s) or	·
	other biological material referred to in	
29-1	the description on:	
29-2	line	99
29-3		24
29-3-1	Identification of Deposit Name of depositary institution	landing Many Culture Collection
29-3-2	Address of depositary institution	American Type Culture Collection
	nadicas of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
29-3-3	Date of deposit	America
29-3-4	Accession Number	25 May 1999 (25.05.1999)
29-4	Additional Indications	ATCC PTA-126
29-4 29-5		NONE
29-5	Designated States for Which Indications are Made	all designated States
29-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
30	the International Bureau later	
30	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
30-1	the description on: page	
30-1	line	99
30-2 30-3		25
30-3 30-3-1	Identification of Deposit Name of depositary institution	Amonican Tymo Cultura Callectica
30-3-2	Address of depositary institution	American Type Culture Collection
		10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
30 3 3	Date of deposit	America
30-3-3	Date of deposit	25 May 1999 (25.05.1999)
30-3-4	6 3 3141	ATCC PTA-128
30-4	Additional Indications	NONE
30-5	Designated States for Which	all designated States

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30-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
31	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
31-1	page	99
31-2	line	26
31-3	Identification of Deposit	
31-3-1	Name of depositary institution	American Type Culture Collection
31-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
31-3-3	Date of deposit	09 February 1999 (09.02.1999)
31-3-4	Accession Number	ATCC 203664
31-4	Additional Indications	NONE
31-5	Designated States for Which Indications are Made	all designated States
31-6	Separate Furnishing of Indications	NONE
· · · · · ·	These indications will be submitted to the International Bureau later	
32	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
32-1	page	99
32-2	line	27
32-3	Identification of Deposit	· · · · · · · · · · · · · · · · · · ·
32-3-1	Name of depositary institution	American Type Culture Collection
32-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
32-3-3	Date of deposit	12 January 1999 (12.01.1999)
32-3-4	Accession Number	ATCC 203578
32-4	Additional Indications	NONE
32-5	Designated States for Which Indications are Made	all designated States
32-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
33	The indications made below relate to the deposited microorganism(s) or	•
	other biological material referred to in the description on:	
33-1	page	99
33-2	line	28
33-3	Identification of Deposit	
33-3-1	Name of depositary institution	American Type Culture Collection
33-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
33-3-3	Date of deposit	22 December 1998 (22.12.1998)
33-3-4	Accession Number	ATCC 203554

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33-4	Additional Indications	NONE
33-5	Designated States for Which Indications are Made	all designated States
33-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
34	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
34-1	page	99
34-2	line	29
34-3	Identification of Deposit	
34-3-1	Name of depositary institution	American Type Culture Collection
34-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	law et a	America
34-3-3	Date of deposit	16 March 1999 (16.03.1999)
34-3-4	Accession Number	ATCC 203850
34-4	Additional Indications	NONE
34-5	Designated States for Which Indications are Made	all designated States
34-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	·
35	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	i other biological material reterred to in	
	the description on:	
35-1		99
35-1 35-2	the description on:	
35-2 35-3	the description on: page line Identification of Deposit	99 30
35-2 35-3 35-3-1	the description on: page line Identification of Deposit Name of depositary institution	99 30 American Type Culture Collection
35-2 35-3	the description on: page line Identification of Deposit	99 30 American Type Culture Collection 10801 University Blvd., Manassas,
35-2 35-3 35-3-1	the description on: page line Identification of Deposit Name of depositary institution	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of
35-2 35-3 35-3-1 35-3-2	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America
35-3 35-3-1 35-3-2 35-3-3	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999)
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-4 35-5	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-4 35-5 35-6	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications Will be submitted to the International Bureau later	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-4 35-5	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The Indications made below relate to the deposited microorganism(s) or	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-4 35-5 35-6	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The Indications made below relate to the deposited microorganism(s) or other biological material referred to in	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-4 35-5 35-6	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The Indications made below relate to the deposited microorganism(s) or	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States NONE
35-2 35-3 35-3-1 35-3-2 35-3-3 35-3-4 35-5 35-6	the description on: page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	99 30 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 May 1999 (11.05.1999) ATCC PTA-45 NONE all designated States

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36-3	Identification of Deposit	
36-3-1	Name of depositary institution	American Type Culture Collection
36-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
36-3-3	Date of deposit	22 December 1998 (22.12.1998)
36-3-4	Accession Number	ATCC 203545
36-4	Additional Indications	
36-5	Designated States for Which	NONE
30-3	Indications are Made	all designated States
36-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
37	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
37-1	page	99
37-2	line	32
37-3	Identification of Deposit	
37-3-1	Name of depositary institution	American Type Culture Collection
37-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
37-3-3	Date of deposit	22 December 1998 (22.12.1998)
37-3-4	Accession Number	ATCC 203544
37-4	Additional Indications	NONE
37-5	Designated States for Which Indications are Made	all designated States
37-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
38	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	·
	the description on:	
38-1	page	99
38-2	line	33
38-3	Identification of Deposit	
38-3-1	Name of depositary institution	American Type Culture Collection
38-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
38-3-3	Date of deposit	15 June 1999 (15.06.1999)
38-3-4	Accession Number	ATCC PTA-234
38-4	Additional Indications	NONE
38-5	Designated States for Which Indications are Made	all designated States
38-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	

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41-5

Designated States for Which

Indications are Made

P3330R1 Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 39-1 page 99 39-2 line 34 39-3 Identification of Deposit 39-3-1 Name of depositary institution American Type Culture Collection 39-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 39-3-3 Date of deposit 16 March 1999 (16.03.1999) 39-3-4 Accession Number ATCC 203848 39-4 Additional Indications NONE 39-5 Designated States for Which all designated States Indications are Made 39-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 40 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 40-1 page 99 40-2 line 35 40-3 Identification of Deposit 40-3-1 Name of depositary institution American Type Culture Collection 40-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 40-3-3 Date of deposit 22 December 1998 (22.12.1998) 40-3-4 Accession Number ATCC 203555 40-4 Additional Indications NONE 40-5 **Designated States for Which** all designated States Indications are Made 40-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 41 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 41-1 page 99 41-2 36 41-3 Identification of Deposit 41-3-1 Name of depositary institution American Type Culture Collection 41-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 41-3-3 Date of deposit 20 April 1999 (20.04.1999) 41-3-4 Accession Number ATCC 203949 41-4 Additional Indications NONE

all designated States

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41-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	HONE
40	the International Bureau later	
42	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
42-1	page	99
42-2	line	37
42-3	Identification of Deposit	
42-3-1	Name of depositary institution	American Type Culture Collection
42-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
42-3-3	Date of deposit	15 December 1998 (15.12.1998)
42-3-4	Accession Number	ATCC 203539
42-4	Additional Indications	NONE
42-5	Designated States for Which Indications are Made	all designated States
42-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	NONE
43	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
43-1	page	99
43-2	line	38.
43-3	Identification of Deposit	
43-3-1	Name of depositary institution	American Type Culture Collection
43-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
43-3-3	Date of deposit	23 March 1999 (23.03.1999)
43-3-4	Accession Number	ATCC 203871
43-4	Additional Indications	NONE
43-5	Designated States for Which Indications are Made	all designated States
43-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
44	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
44-1	page	99
44-2	line	39
44-3	Identification of Deposit	
44-3-1	Name of depositary institution	American Type Culture Collection
44-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of
44-3-3	Date of deposit	America
44-3-4	Accession Number	23 March 1999 (23.03.1999)
	Association (Author)	ATCC 203862

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44-4	Additional Indications	NONE
44-5	Designated States for Which Indications are Made	all designated States
44-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	·
45	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	·
45-1 45-2	page	99
45-2	line	40
45-3 45-3-1	Identification of Deposit Name of depositary institution	American Marco Cultura Callactica
45-3-2	Address of depositary institution	American Type Culture Collection
	ratios or especially monation	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
45-3-3	Date of deposit	
45-3-4	Accession Number	10 August 1999 (10.08.1999) ATCC PTA-510
45-4	Additional Indications	NONE
45-5	Designated States for Which	
	Indications are Made	all designated States
45-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
46	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
46-1	page	99
46-2	line	41
46-3	Identification of Deposit	
46-3-1	Name of depositary institution	American Type Culture Collection
46-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
•		America
46-3-3	Date of deposit	20 January 1999 (20.01.1999)
46-3-4	Accession Number	ATCC 203603
46-4	Additional Indications	NONE
46-5	Designated States for Which Indications are Made	all designated States
46-6		NONE
	These indications will be submitted to the International Bureau later	
47	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
47-1	page	99
47-2	line	42
		

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47-3	Identification of Deposit	
47-3-1	Name of depositary institution	American Type Culture Collection
47-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
47-3-3	Date of deposit	02 March 1999 (02.03.1999)
47-3-4	Accession Number	ATCC 203813
47-4	Additional Indications	NONE
47-5	Designated States for Which	all designated States
47-6	Indications are Made Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	NONE
48	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
48-1	page	99
48-2	line	43
48-3	Identification of Deposit	
48-3-1	Name of depositary institution	American Type Culture Collection
48-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
40.00		America
48-3-3	Date of deposit	02 March 1999 (02.03.1999)
48-3-4	Accession Number	ATCC 203812
48-4	Additional Indications	NONE
48-5	Designated States for Which Indications are Made	all designated States
48-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
49	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
49-1	page	99
49-2	line	44
49-3	Identification of Deposit	
49-3-1	Name of depositary institution	American Type Culture Collection
49-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
49-3-3	Date of deposit	29 October 1998 (29.10.1998)
49-3-4	Accession Number	ATCC 203391
49-4	Additional Indications	NONE
49-5	Designated States for Which Indications are Made	all designated States
49-6	O	NONE
	These indications will be submitted to the International Bureau later	

50		DIMISSION) - PINILEG ON 01.12.2000 02.37.33 FIVI
50	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	·
50-1	page	99
50-2	line	45
50-3	Identification of Deposit	
50-3-1	Name of depositary institution	American Type Culture Collection
50-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
50-3-3	Date of deposit	27 April 1999 (27.04.1999)
50-3-4	Accession Number	ATCC 203965
50-4	Additional Indications	NONE
50-5	Designated States for Which	
	Indications are Made	all designated States
50-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
51	the International Bureau later	
וס	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
51-1	page	99
51-2	line	46
51-3	Identification of Deposit	
51-3-1	Name of depositary institution	American Type Culture Collection
51-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
51-3-3	Date of deposit	02 March 1999 (02.03.1999)
51-3-4	Accession Number	ATCC 203816
51-4	Additional Indications	NONE
51-5	Designated States for Which	all designated States
	Indications are Made	all doolghaced beaces
51-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	·
52	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
52-1	page	99
52-2	line	
52-3	Identification of Deposit	47
52-3-1	Manage 4	Amenican Muna Cultume C-11
52-3-2	Address of depositary institution	American Type Culture Collection
	,	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
5000	1	America
52-3-3	Date of deposit	02 March 1999 (02.03.1999)
52-3-4		ATCC 203814
52-4	Additional Indications	NONE
52-5	Designated States for Which	all designated States
	Indications are Made	

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52-6	Separate Furnishing of Indications	Trong.
	These indications will be submitted to	NONE
	the International Bureau later	
53	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
53-1	page	99
53-2	line	48
53-3	Identification of Deposit	
53-3-1	Name of depositary institution '	American Type Culture Collection
53-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
53-3-3	Date of deposit	02 March 1999 (02.03.1999)
53-3-4	Accession Number	ATCC 203810
53-4	Additional Indications	NONE
53-5	Designated States for Which	all designated States
	Indications are Made	all designated states
53-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
54	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
54-1	page	99
54-2	line	49
54-3	Identification of Deposit	
54-3-1	Name of depositary institution	American Type Culture Collection
54-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
54-3-3	Date of deposit	04 May 1999 (04.05.1999)
54-3-4	Accession Number	ATCC PTA-22
54-4	Additional Indications	NONE
54-5	Designated States for Which	all designated States
	Indications are Made	all designated states
54-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
55	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
55-1	page	99
55-2	line	50
55-3	Identification of Deposit	
55-3-1	Name of depositary institution	American Type Culture Collection
55-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
55-3-3	Date of deposit	12 January 1999 (12.01.1999)
55-3-4	Accession Number	ATCC 203580
	l	MICC 203300

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55-4	Additional Indications	NONE
55-5	Designated States for Which	all designated States
55-6	Indications are Made Separate Furnishing of Indications	
00-0	These indications will be submitted to	NONE
	the International Bureau later	
56	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
56-1	the description on:	
56-2	line	99
56-3	Identification of Deposit	51
56-3-1	Name of depositary institution	American Type Culture Collection
56-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
56-3-3	Date of deposit	30 March 1999 (30.03.1999)
56-3-4	Accession Number	ATCC 203889
56-4	Additional Indications	NONE
56-5	Designated States for Which Indications are Made	all designated States
56-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
57	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
57-1	page	99
57-2	line	52
57-3	14-48	
	Identification of Deposit	
57-3-1	Name of depositary institution	American Type Culture Collection
57-3-1 57-3-2		10801 University Blvd., Manassas,
	Name of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of
57-3-2	Name of depositary institution Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
57-3-2 57-3-3	Name of depositary institution Address of depositary institution Date of deposit	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999)
57-3-2	Name of depositary institution Address of depositary institution Date of deposit Accession Number	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964
57-3-2 57-3-3 57-3-4	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE
57-3-2 57-3-3 57-3-4 57-4 57-5	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964
57-3-2 57-3-3 57-3-4	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE
57-3-2 57-3-3 57-3-4 57-4 57-5	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE all designated States
57-3-2 57-3-3 57-3-4 57-4 57-5	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE all designated States
57-3-2 57-3-3 57-3-4 57-4 57-5 57-6	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE all designated States
57-3-2 57-3-3 57-3-4 57-4 57-5 57-6	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE all designated States NONE
57-3-2 57-3-3 57-3-4 57-4 57-5 57-6	Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page	10801 University Blvd., Manassas, Virginia 20110-2209United States of America 27 April 1999 (27.04.1999) ATCC 203964 NONE all designated States

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58-3	Identification of Descrip	
58-3-1	Identification of Deposit Name of depositary institution	Amorican Culture Callesties
58-3-2	Address of depositary institution	American Type Culture Collection
	radios of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
58-3-3	Date of deposit	America
58-3-4	Accession Number	22 December 1998 (22.12.1998)
58-4	Additional Indications	ATCC 203548
58-5		NONE
20-2	Designated States for Which Indications are Made	all designated States
58-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
59	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
59-1	page	99
59-2	line	54
59-3	Identification of Deposit	
59-3-1	Name of depositary institution	American Type Culture Collection
59-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	İ	Virginia 20110-2209United States of
		America
59-3-3	Date of deposit	02 March 1999 (02.03.1999)
59-3-4	Accession Number	ATCC 203817
59-4	Additional Indications	NONE
59-5	Designated States for Which Indications are Made	all designated States
59-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
60	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
60-1	page	00
60-2	line	99
60-3	Identification of Deposit	55
60-3-1	Name of depositary institution	American Type Culture Collection
60-3-2	Address of depositary institution	10801 University Blvd., Manassas,
-		Virginia 20110-2209United States of
	,	America
60-3-3	Date of deposit	1
60-3-4	Accession Number	15 June 1999 (15.06.1999)
60-4	Additional Indications	ATCC PTA-235
60-5	Designated States for Which	NONE
	Indications are Made	all designated States
60-6		NONE
	These indications will be submitted to	
	the International Bureau later	,

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61	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
61-1	page	100
61-2	line	2
61-3	Identification of Deposit	
61-3-1	Name of depositary institution	American Type Culture Collection
61-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
61-3-3	Date of deposit	27 April 1999 (27.04.1999)
61-3-4	Accession Number	ATCC 203968
61-4	Additional Indications	NONE
61-5	Designated States for Which	all designated States
C4 ^	Indications are Made	
61-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
62	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
62-1	page	100
62-2	line	3
32-3	Identification of Deposit	
52-3-1	Name of depositary institution	American Type Culture Collection
62-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
62-3-3	Date of deposit	30 March 1999 (30.03.1999)
62-3-4	Accession Number	ATCC 203894
62-4	Additional Indications	NONE
62-5	Designated States for Which Indications are Made	all designated States
52-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
53	the International Bureau later The indications made below relate to	
-	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
33-1	page	100
53-2	line	4
33-3	Identification of Deposit	
3-3-1	la. a	American Type Culture Collection
33-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
3-3-3	Date of deposit	30 March 1999 (30.03.1999)
3-3-4	Accession Number	ATCC 203893
3-4	A -4 -1949 1 A - 19 4	NONE
3-5	Designated States for Which	all designated States
	Indications are Made	all addagnadaa daada

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63-6	Separate Furnishing of Indications	INONE
	These indications will be submitted to	NONE
	the International Bureau later	
64	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	·
64-1	page	100
64-2	line	5
64-3	Identification of Deposit	
64-3-1	Name of depositary institution	American Type Culture Collection
64-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
64-3-3	Date of deposit	02 March 1999 (02.03.1999)
64-3-4	Accession Number	ATCC 203811
64-4	Additional Indications	NONE
64-5	Designated States for Which Indications are Made	all designated States
64-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
65	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
65-1	page	100
65-2	line	6
65-3	Identification of Deposit	
65-3-1	Name of depositary institution	American Type Culture Collection
65-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
65-3-3	Date of deposit	23 March 1999 (23.03.1999)
65-3-4	Accession Number	ATCC 203867
65-4	Additional Indications	NONE
65-5	Designated States for Which	all designated States
	Indications are Made	
65-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
66	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
66-1	page	100
66-2	line	7
66-3	Identification of Deposit	
66-3-1	Name of depositary institution	American Type Culture Collection
66-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
66-3-3	Date of deposit	27 April 1999 (27.04.1999)
66-3-4	Accession Number	ATCC 203963

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66-4	Additional Indications	NONE
66-5	Designated States for Which Indications are Made	all designated States
66-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
67	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
67-1	page	100
67-2	line	8
67-3	Identification of Deposit	
67-3-1	Name of depositary institution	American Type Culture Collection
67-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
67-3-3	Date of deposit	02 March 1999 (02.03.1999)
67-3-4	Accession Number	ATCC 203815
67-4	Additional Indications	NONE
67-5	Designated States for Which Indications are Made	all designated States
67-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
68	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
68-1	page	100
68-2	line	9
68-3	Identification of Deposit	
68-3-1	Name of depositary institution	American Type Culture Collection
68-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
68-3-3	Date of deposit	30 March 1999 (30.03.1999)
68-3-4	Accession Number	ATCC 203890
68-4	Additional Indications	NONE
68-5	Designated States for Which Indications are Made	all designated States
68-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
69	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
69 69-1	the deposited microorganism(s) or other biological material referred to in	100

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Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM 69-3 Identification of Deposit 69-3-1 Name of depositary institution American Type Culture Collection 69-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 69-3-3 Date of deposit 25 May 1999 (25.05.1999) 69-3-4 Accession Number ATCC PTA-130 69-4 Additional Indications NONE 69-5 Designated States for Which all designated States Indications are Made 69-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 70 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 70-1 page 100 70-2 line 11 70-3 Identification of Deposit 70-3-1 Name of depositary institution American Type Culture Collection 70-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 70-3-3 Date of deposit 27 April 1999 (27.04.1999) 70-3-4 Accession Number ATCC 203970 70-4 Additional Indications NONE 70-5 **Designated States for Which** all designated States Indications are Made 70-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 71 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 71-1 page 100 71-2 12 71-3 Identification of Deposit 71-3-1 Name of depositary institution American Type Culture Collection 71-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 71-3-3 Date of deposit 16 March 1999 (16.03.1999) 71-3-4 Accession Number ATCC 203845 71-4 Additional Indications NONE Designated States for Which 71-5 all designated States Indications are Made 71-6 Separate Furnishing of Indications NONE These indications will be submitted to

the International Bureau later

72	The indications made below relate to	T
12	the deposited microorganism(s) or	
	other biological material referred to in	
72-1	the description on:	100
72-2	line	100
72-3	Identification of Deposit	13
72-3-1	Name of depositary institution	American Type Culture Collection
72-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	,	Virginia 20110-2209United States of
		America
72-3-3	Date of deposit	23 March 1999 (23.03.1999)
72-3-4	Accession Number	ATCC 203861
72-4	Additional Indications	<u></u>
72-5	Designated States for Which	NONE
72-0	Indications are Made	all designated States
72-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
73	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in	·
73-1	the description on:	100
73-2	line	114
73-3	Identification of Deposit	14
73-3-1	Name of depositary institution	American Type Culture Collection
73-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
73-3-3	Date of deposit	16 March 1999 (16.03.1999)
73-3-4	Accession Number	ATCC 203844
73-4	Additional Indications	NONE
73-5	Designated States for Which	all designated States
	Indications are Made	arr addramated blades
73-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
74	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
74-1	page	100
74-2	line	15
74-3	Identification of Deposit	·
74-3-1	Name of depositary institution	American Type Culture Collection
74-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
74-3-3	Date of deposit	10 August 1999 (10.08.1999)
74-3-4	Accession Number	ATCC PTA-513
74-4	Additional Indications	NONE
74-5	Designated States for Which	all designated States
	Indications are Made	

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74-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
75	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
7 5 -1	page	100
75-2	line	16
75-3	Identification of Deposit	
75-3-1	Name of depositary institution	American Type Culture Collection
75-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
75-3-3	Date of deposit	09 February 1999 (09.02.1999)
75-3-4	Accession Number	ATCC 203663
75-4	Additional Indications	NONE
75-5	Designated States for Which	all designated States
75-6	Indications are Made Separate Furnishing of Indications	
75-0	1 '	NONE
	These indications will be submitted to the International Bureau later	
76	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
76-1	page	100
76-2	line .	17
76-3	Identification of Deposit	
76-3-1	Name of depositary institution	American Type Culture Collection
76-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	<u></u>	America
76-3-3	Date of deposit	16 March 1999 (16.03.1999)
76-3-4 	Accession Number	ATCC 203851
76-4	Additional Indications	NONE
76-5	Designated States for Which Indications are Made	all designated States
76-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
77	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
77-1	page	100
77-2	line	18
77-3 77-3-1	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
77-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
77-3-3	Date of deposit	20 April 1999 (20.04.1999)
77-3-4	Accession Number	ATCC 203950

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77-4	Additional Indications	NONE
77-5	Designated States for Which	all designated States
77-6	Indications are Made	
11-0	Separate Furnishing of Indications These indications will be submitted to	NONE
	the International Bureau later	
78	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
78-1	page	100
78-2	line	19
78-3 78-3-1	Identification of Deposit Name of depositary institution	
78-3-2	Address of depositary institution	American Type Culture Collection
70-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
78-3-3	Date of deposit	America
78-3-4	Accession Number	30 March 1999 (30.03.1999)
78-4	Additional Indications	ATCC 203895
78-5	Designated States for Which	NONE
70-5	Indications are Made	all designated States
78-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
79	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
79-1	page	100
79-2	line	20
79-3	Identification of Deposit	
79-3-1	Name of depositary institution	American Type Culture Collection
79-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
79-3-3	Date of deposit	25 May 1999 (25.05.1999)
79-3-4	Accession Number	ATCC PTA-134
79-4	Additional Indications	NONE
79-5	Designated States for Which Indications are Made	all designated States
79-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	at Value
	the International Bureau later	
80	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
00.4	the description on:	
80-1	page	100
80-2	line	21

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P3330R1 Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM 80-3 Identification of Deposit 80-3-1 Name of depositary institution American Type Culture Collection 80-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 80-3-3 Date of deposit 16 March 1999 (16.03.1999) 80-3-4 Accession Number ATCC 203852 80-4 **Additional Indications** NONE 80-5 **Designated States for Which** all designated States Indications are Made 80-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 81-1 page 100 81-2 line 22 81-3 Identification of Deposit 81-3-1 Name of depositary institution American Type Culture Collection 81-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 81-3-3 Date of deposit 22 June 1999 (22.06.1999) 81-3-4 Accession Number ATCC PTA-258 81-4 Additional Indications NONE 81-5 **Designated States for Which** all designated States Indications are Made 81-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 82 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 82-1 page 100 82-2 23 **B2-3** Identification of Deposit 82-3-1 Name of depositary institution American Type Culture Collection 82-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 82-3-3 Date of deposit 22 June 1999 (22.06.1999) 82-3-4 Accession Number ATCC PTA-259 82-4 Additional Indications NONE 82-5 **Designated States for Which** all designated States Indications are Made 82-6 Separate Furnishing of Indications NONE

These indications will be submitted to the International Bureau later

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83	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
83-1	page	100
83-2	line	24
83-3	Identification of Deposit	
83-3-1	Name of depositary institution	American Type Culture Collection
83-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
83-3-3	Date of deposit	23 March 1999 (23.03.1999)
83-3-4	Accession Number	ATCC 203866
83-4	Additional Indications	NONE
83-5	Designated States for Which	all designated States
83-6	Indications are Made	
03-0	Separate Furnishing of Indications	NONE
•	These indications will be submitted to the International Bureau later	
84	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
84-1	page	100
84-2	line	25
84-3	Identification of Deposit	
84-3-1	Name of depositary institution	American Type Culture Collection
84-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
84-3-3	Date of deposit	16 March 1999 (16.03.1999)
84-3-4	Accession Number	ATCC 203853
84-4	Additional Indications	NONE
84-5	Designated States for Which Indications are Made	all designated States
84-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
85	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
85-1	page	100
85-2	line	26
85-3	Identification of Deposit	
85-3-1	Name of depositary institution	American Type Culture Collection
85-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
85-3-3	Date of deposit	30 March 1999 (30.03.1999)
85-3-4	Accession Number	ATCC 203892
85-4	Additional Indications	NONE
85-5	Designated States for Which	all designated States
	Indications are Made	

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85-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	INVIE
	the International Bureau later	
86	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
86-1	page	100
86-2	line	27
86-3	Identification of Deposit	
86-3-1	Name of depositary institution	American Type Culture Collection
86-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
86-3-3	Date of deposit	16 March 1999 (16.03.1999)
86-3-4	Accession Number	ATCC 203847
86-4	Additional Indications	NONE
86-5	Designated States for Which Indications are Made	all designated States
86-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
87	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
87-1	page	100
87-2	line	28
87-3	Identification of Deposit	
87-3-1	Name of depositary institution	American Type Culture Collection
87-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
87-3-3	Date of deposit	04 May 1999 (04.05.1999)
87-3-4	Accession Number	ATCC PTA-21
87-4	Additional Indications	NONE
87-5	Designated States for Which	all designated States
87-6	Indications are Made	
07-0	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
88	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
88-1	page	100
88-2	line	29
38-3	Identification of Deposit	
38-3-1	Name of depositary institution	American Type Culture Collection
38-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
38-3-3	Date of deposit	25 May 1999 (25.05.1999)
B8-3-4	Accession Number	ATCC PTA-121

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88-4	Additional Indications	NONE
88-5	Designated States for Which Indications are Made	all designated States
88-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
89	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
89-1	page	100
89-2	line	30
89-3 89-3-1	Identification of Deposit Name of depositary institution	
89-3-2	Address of depositary institution	American Type Culture Collection
03-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
89-3-3	Date of deposit	America
89-3-4	Accession Number	20 April 1999 (20.04.1999)
89-4		ATCC 203951
89-5	Additional Indications	NONE
03-0	Designated States for Which Indications are Made	all designated States
89-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
90	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
90-1	page	100
90-2	line	31
90-3	Identification of Deposit	
90-3-1	Name of depositary institution	American Type Culture Collection
90-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
90-3-3	Date of deposit	23 March 1999 (23.03.1999)
90-3-4	Accession Number	ATCC 203869
90-4	Additional Indications	NONE
90-5	Designated States for Which Indications are Made	all designated States
90-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
91	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
91-1	page	100
91-2	1	32

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91-3	Identification of Deposit	
91-3-1	Name of depositary institution	American Type Culture Collection
91-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	i dances or copesitary montation	1
		Virginia 20110-2209United States of
91-3-3	Date of deposit	America
91-3-4	Accession Number	15 June 1999 (15.06.1999)
91-4		ATCC PTA-232
	Additional Indications	NONE
91-5	Designated States for Which Indications are Made	all designated States
91-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
92	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
92-1	page	100
92-2	line	33
92-3	Identification of Deposit	
92-3-1	Name of depositary institution	American Type Culture Collection
92-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	·	America
92-3-3	Date of deposit	20 July 1999 (20.07.1999)
92-3-4	Accession Number	ATCC PTA-385
92-4	Additional Indications	NONE
92-5	Designated States for Which Indications are Made	all designated States
92-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
93	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
93-1	page	100
93-2	line	34
93-3 93-3-1	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
55 5 2	rearess or deposits y institution	10801 University Blvd., Manassas,
	İ	Virginia 20110-2209United States of
93-3-3	Date of deposit	America
93-3-4	Accession Number	23 March 1999 (23.03.1999)
93-3-4	Additional Indications	ATCC 203864
93-4		NONE
	Designated States for Which Indications are Made	all designated States
93-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
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94	The indications made below relate to	T
	the deposited microorganism(s) or other biological material referred to in the description on:	
94-1	page	100
94-2	line	1
94-3		35
94-3-1	Identification of Deposit Name of depositary institution	American Type Culture Collection
94-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
94-3-3	Date of deposit	22 June 1999 (22.06.1999)
94-3-4	Accession Number	ATCC PTA-262
94-4	Additional Indications	NONE
94-5	Designated States for Which	all designated States
04.6	Indications are Made	
94-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
95	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
95-1	page	100
95-2	line	36
5-3	Identification of Deposit	
95-3-1	Name of depositary institution	American Type Culture Collection
95-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
95-3-3	Date of deposit	20 July 1999 (20.07.1999)
95-3-4	Accession Number	ATCC PTA-381
95-4	Additional Indications	NONE
95-5	Designated States for Which Indications are Made	all designated States
95-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
96	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
96-1	page	100
96-2	line	37
6-3	Identification of Deposit	
6-3-1	Name of depositary institution	American Type Culture Collection
6-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
6-3-3	Date of deposit	04 May 1999 (04.05.1999)
16-3-4	Accession Number	ATCC PTA-15
96-4	Additional Indications	NONE
6-5	Designated States for Which	all designated States
	Indications are Made	

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	·	
96-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
-07	the International Bureau later	
97	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
97-1	page	100
97-2	line	38
97-3	Identification of Deposit	
97-3-1	Name of depositary institution	American Type Culture Collection
97-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
97-3-3	Date of deposit	15 June 1999 (15.06.1999)
97-3-4	Accession Number	ATCC PTA-239
97-4	Additional Indications	NONE
97-5	Designated States for Which	
	Indications are Made	all designated States
97-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
98	the International Bureau later The indications made below relate to	
30	the deposited microorganism(s) or	
	other biological material referred to in	
00.4	the description on:	
98-1	page 	100
98-2	line	39
98-3 98-3-1	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
98-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
98-3-3	Date of deposit	20 July 1999 (20.07.1999)
98-3-4	Accession Number	ATCC PTA-384
98-4	Additional Indications	NONE
98-5	Designated States for Which	all designated States
00.0	Indications are Made	
98-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
99	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
99-1	page	100
99-2	line	100
99-3		40
99-3 99-3-1	Identification of Deposit Name of depositary institution	Amondana Maria Children City
99-3-2	Address of depositary institution	American Type Culture Collection
33-J-Z	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	1	America
99-3-3	Date of deposit	03 August 1999 (03.08.1999)
99-3-4	Accession Number	ATCC PTA-475

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99-4	Additional Indications	NONE
99-5	Designated States for Which	all designated States
	Indications are Made	
99-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
100	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
100-1	the description on:	
100-1	line	100
100-2	Identification of Deposit	41
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	
.0002	*	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
100-3-3	Date of deposit	16 March 1999 (16.03.1999)
	Accession Number	
100-4	Additional Indications	ATCC 203854 NONE
100-5	Designated States for Which	
	Indications are Made	all designated States
100-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
101	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
101-1	page	100
101-2	line	42
101-3	Identification of Deposit	
101-3-1	Name of depositary institution	American Type Culture Collection
101-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	į	America
101-3-3	Date of deposit	20 July 1999 (20.07.1999)
101-3-4	Accession Number	ATCC PTA-378
101-4	Additional Indications	NONE
101-5	Designated States for Which Indications are Made	all designated States
101-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
102	the International Bureau later	
102	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
102-1	the description on:	
	line	100
102-2		43

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102-3	Identification of Deposit	
102-3-1	Name of depositary institution	American Type Culture Collection
102-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
102-3-3	Date of deposit	22 June 1999 (22.06.1999)
	Accession Number	ATCC PTA-257
102-4	Additional Indications	
102-5	Designated States for Which	NONE
	Indications are Made	all designated States
102-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
103	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	·
	the description on:	
103-1	page ·	100
103-2	line	44
103-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
103-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
103-3-3	Date of deposit	15 June 1999 (15.06.1999)
103-3-4	Accession Number	ATCC PTA-231
103-4	Additional Indications	NONE
103-5	Designated States for Which Indications are Made	all designated States
103-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
104	the International Bureau later The indications made below relate to	
·	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
104-1	page	100
104-2	line	45
104-3	Identification of Deposit	34
-	Name of depositary institution	American Type Culture Collection
104-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	•	Virginia 20110-2209United States of
		America
104-3-3	Date of deposit	20 July 1999 (20.07.1999)
104-3-4	Accession Number	ATCC PTA-388
104-4	Additional Indications	NONE
104-5	Designated States for Which	all designated States
	Indications are Made	all acolynated beated
104-6		NONE
	These indications will be submitted to the International Bureau later	

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105-1 page 105-2 line 105-3 Identification of Deposit 105-3-1 Name of depositary institution 105-3-2 Address of depositary institution 105-3-2 Address of depositary institution 10801 University Blvd., Manassas,	
105-3 105-3-1 Name of depositary institution 105-3-2 Address of depositary institution 105-3-2 Name of depositary institution 10801 University Blvd., Manassas,	
Name of depositary institution Address of depositary institution American Type Culture Collection 105-3-2 Address of depositary institution 10801 University Blvd., Manassas,	
105-3-2 Address of depositary institution 10801 University Blvd., Manassas,	
10001 oniversity bive., ramessus,	
Virginia 20110-2209United States of	
America	
105-3-3 Date of deposit 31 August 1999 (31.08.1999)	
105-3-4 Accession Number ATCC PTA-620	
105-4 Additional Indications NONE	
Designated States for Which all designated States Indications are Made	
105-6 Separate Furnishing of Indications NONE	
These indications will be submitted to the International Bureau later	
The indications made below relate to the deposited microorganism(s) or	
other biological material referred to in	
the description on:	
106-1 page 100	
106-2 line 47	
106-3 Identification of Deposit 106-3-1 Name of depositary institution American Type Culture Collection	
randridan typo darbard dollars.	
20001 ChityClbicy Diva., Limitabas,	i
Virginia 20110-2209United States of America	
106-3-3 Date of deposit 25 May 1999 (25.05.1999)	
106-3-4 Accession Number ATCC PTA-118	
106-4 Additional Indications NONE	
106-5 Designated States for Which all designated States	
Indications are Made	
106-6 Separate Furnishing of Indications NONE	
These indications will be submitted to the International Bureau later	
107 The indications made below relate to	
the deposited microorganism(s) or other biological material referred to in	
the description on:	
107-1 page 100	
107-2 line	
107-3 Identification of Deposit	
107-3-1 Name of depositary institution American Type Culture Collection	
107-3-2 Address of depositary institution 10801 University Blvd., Manassas,	
Virginia 20110-2209United States of	
America	
107-3-3 Date of deposit 03 August 1999 (03.08.1999)	
107-3-4 Accession Number ATCC PTA-477	
107-4 Additional Indications NONE	
107-5 Designated States for Which Indications are Made all designated States	

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107-6	Separate Furnishing of Indications	
101-0	These indications will be submitted to	NONE
	the International Bureau later	
108	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
108-1	page	100
108-2	line	49
108-3	Identification of Deposit Name of depositary institution	
	-	American Type Culture Collection
100-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
100 2 2	Data of dance it	America
	Date of deposit	03 August 1999 (03.08.1999)
108-3-4		ATCC PTA-488
108-4	Additional Indications	NONE
100-5	Designated States for Which Indications are Made	all designated States
108-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
109	The Indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
109-1	page	100
109-2	line	50
109-3	Identification of Deposit Name of depositary institution	
	l -	American Type Culture Collection
103-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
100 2 2	Data of demonit	America
	Date of deposit Accession Number	16 March 1999 (16.03.1999)
109-3-4	Additional Indications	ATCC 203849
109-5		NONE
109-6	Designated States for Which Indications are Made	all designated States
109-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	·
110	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
110-1	page	100
110-2	line	51
110-3	Identification of Deposit	
110-3-1	,	American Type Culture Collection
110-3-2	Address of depositary institution	10801 University Blvd., Manassas,
i		Virginia 20110-2209United States of
		America
110-3-3		09 March 1999 (09.03.1999)
110-3-4	Accession Number	ATCC 203837

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110-4	Additional Indications	NONE
110-5	Designated States for Which	all designated States
110-6	Indications are Made Separate Furnishing of Indications	
110-0	These indications will be submitted to	NONE
	the International Bureau later	
111	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
111-1	page	100
111-2	line	52
111-3	Identification of Deposit Name of depositary institution	
	•	American Type Culture Collection
111-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	,	Virginia 20110-2209United States of
111-3-3	Date of deposit	America
	Accession Number	20 July 1999 (20.07.1999)
111-3-4	L.	ATCC PTA-380
111-4	Additional Indications	NONE
111-5	Designated States for Which Indications are Made	all designated States
111-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
112	the International Bureau later The Indications made below relate to	
•••	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
112-1	page	100
112-2	line	53
112-3	Identification of Deposit	33
112-3-1	Name of depositary institution	American Type Culture Collection
112-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
112-3-3	Date of deposit	11 May 1999 (11.05.1999)
112-3-4	Accession Number	ATCC PTA-44
112-4	Additional Indications	NONE
	Designated States for Which	all designated States
	Indications are Made Separate Furnishing of Indications	NONE
-	These indications will be submitted to	NONE
	the International Bureau later	
	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
. 1	the description on:	
1		100
113-2	line	54

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	1	
113-3	Identification of Deposit Name of depositary institution	
	· · ·	American Type Culture Collection
113-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
113-3-3	Date of deposit	11 May 1999 (11.05.1999)
113-3-4	Accession Number	ATCC PTA-42
113-4	Additional Indications	NONE
113-5	Designated States for Which Indications are Made	all designated States
113-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
114	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
114-1	page	100
114-2	line	55
114-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
114-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
114-3-3	Date of deposit	25 May 1999 (25.05.1999)
114-3-4	Accession Number	ATCC PTA-123
114-4	Additional Indications	NONE
114-5	Designated States for Which Indications are Made	all designated States
114-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
115	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
115-1	page 	101
115-2	line	2
115-3	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
113-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
115-3-3	Date of deposit	03 August 1999 (03.08.1999)
115-3-4	Accession Number	ATCC PTA-482
115-4	Additional Indications	NONE .
115-5	Designated States for Which	all designated States
445.5	Indications are Made	
115-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
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116	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
116-1	page	101
116-2	line	3
116-3	Identification of Deposit	
116-3-1	Name of depositary institution	American Type Culture Collection
116-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
116-3-3	Date of deposit	03 August 1999 (03.08.1999)
116-3-4	Accession Number	ATCC PTA-483
116-4	Additional Indications	NONE
116-5	Designated States for Which	all designated States
116-6	Indications are Made Separate Furnishing of Indications	
	These indications will be submitted to	NONE
	the International Bureau later	
117	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
117-1	page	101
117-2	line	4
117-3	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
117-5-2	Tradiess of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
117-3-3	Date of deposit	America
	Accession Number	03 August 1999 (03.08.1999)
117-4	Additional Indications	ATCC PTA-485
117-5	Designated States for Which	NONE
	Indications are Made	all designated States
117-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
118	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
118-1	page	101
118-2	line	5
118-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
118-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
118-3-3	Date of deposit	03 August 1999 (03.08.1999)
	Accession Number	ATCC PTA-480
118-4	Additional Indications	NONE
118-5	Designated States for Which	all designated States
	Indications are Made	-

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118-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
119	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
110.4	the description on:	
119-1 119-2	page .	101
119-3	Identification of Deposit	6
	Name of depositary institution	American Type Culture Collection
119-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
119-3-3	Date of deposit	03 August 1999 (03.08.1999)
	Accession Number	ATCC PTA-476
119-4	Additional Indications	NONE
119-5	Designated States for Which Indications are Made	all designated States
119-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
120	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
120-1	page	101
120-2	line	7
120-3 120-3-1	Identification of Deposit	
	Name of depositary institution Address of depositary institution	American Type Culture Collection
120-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
120-3-3	Date of deposit	America 03 August 1999 (03.08.1999)
120-3-4	Accession Number	ATCC PTA-472
120-4	Additional Indications	NONE
120-5	Designated States for Which	all designated States
120-6	Indications are Made Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
121	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
121-1	the description on:	101
121-2	line	101 8
121-3	Identification of Deposit	•
	Name of depositary institution	American Type Culture Collection
121-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	03 August 1999 (03.08.1999)
121-3-4	Accession Number	ATCC PTA-487

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121-4	Additional Indications	NONE
121-5	Designated States for Which Indications are Made	all designated States
121-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
122	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
122-1	page	101
122-2	line	9
122-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
122-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
122-3-3	Date of deposit	03 August 1999 (03.08.1999)
122-3-4	Accession Number	ATCC PTA-484
122-4	Additional Indications	NONE
122-5	Designated States for Which Indications are Made	all designated States
122-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
123	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
123-1	page 	101
123-2	line	10
123-3 123-3-1	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
.2002	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
123-3-3	Date of deposit	America
	Accession Number	17 August 1999 (17.08.1999) ATCC PTA-546
123-4	Additional Laboration	NONE
123-5	Designated States for Which	all designated States
123-6	Indications are Made Separate Furnishing of Indications	
	These indications will be submitted to	NONE
_	the International Bureau later	
	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
124-1	page	101
124-2	line	11

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124-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	
,	ridaress or depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
124-3-3	Date of deposit	America
	Accession Number	10 August 1999 (10.08.1999)
124-3-4		ATCC PTA-515
	Additional Indications	NONE
124-5	Designated States for Which Indications are Made	all designated States
124-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
125	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
125-1	page	101
125-2	line	12
125-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
125-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
125-3-3	Date of deposit	19 October 1999 (19.10.1999)
25-3-4	Accession Number	ATCC PTA-861
25-4	Additional Indications	NONE
125-5	Designated States for Which Indications are Made	all designated States
125-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
126	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
126-1	page	101
126-2	line	13
26-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
26-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
26-3-3	Date of deposit	10 August 1999 (10.08.1999)
26-3-4	Accession Number	ATCC PTA-518
26-4	Additional Indications	NONE
126-5	Designated States for Which Indications are Made	all designated States
126-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	

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127	The indications made below relate to the deposited microorganism(s) or other biological material referred to in	
	the description on:	
127-1	page	101
127-2	line	14
127-3	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
127-0-2	Address of depositary institution	10801 University Blvd., Manassas,
	*	Virginia 20110-2209United States of America
127-3-3	Date of deposit	10 August 1999 (10.08.1999)
127-3-4	Accession Number	ATCC PTA-512
127-4	Additional Indications	NONE
127-5	Designated States for Which	all designated States
127-6	Indications are Made Separate Furnishing of Indications	
121-0	These indications will be submitted to	NONE
	the International Bureau later	,
128	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
128-1	page	101
128-2	line	15
128-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
128-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	03 August 1999 (03.08.1999)
	Accession Number	ATCC PTA-489
128-4	Additional Indications	NONE
128-5	Designated States for Which Indications are Made	all designated States
128-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
129	the International Bureau later The indications made below relate to	
123	the deposited microorganism(s) or other biological material referred to in the description on:	
129-1	page	101
129-2	line	16
129-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
129-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
i	Date of deposit	31 August 1999 (31.08.1999)
		ATCC PTA-614
129-4		NONE
129-5	Designated States for Which Indications are Made	all designated States

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129-6	Separate Furnishing of Indications	Tyron Tyron
120-0		NONE
	These indications will be submitted to the International Bureau later	
130	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
130-1	page	101
130-2	line	17
130-3	Identification of Deposit	
130-3-1		American Type Culture Collection
130-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
130-3-3	Date of deposit	1
	Accession Number	16 November 1999 (16.11.1999)
130-4	Additional Indications	ATCC PTA-957
130-5		NONE
130-3	Designated States for Which Indications are Made	all designated States
130-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
454	the International Bureau later	
131	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	·
131-1	page	101
131-2	line	
131-3 131-3-1	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
131-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	05 October 1999 (05.10.1999)
	Accession Number	ATCC PTA-819
131-4	Additional Indications	NONE
131-5	Designated States for Which	all designated States
131-6	Indications are Made Separate Furnishing of Indications	NONE
- · ·	These indications will be submitted to	NONE
	the International Bureau later	
132	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
132-1	page	101
132-2	line	19
132-3	Identification of Deposit	
132-3-1	Name of depositary institution	American Type Culture Collection
132-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
132-3-3	Date of deposit	18 September 1997 (18.09.1997)
132-3-4	Accession Number	ATCC 209280
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132-4	Additional Indications	NONE
132-5	Designated States for Which	all designated States
400.0	Indications are Made	
132-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
133	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
133-1	page	101
133-2	line	20
133-3	Identification of Deposit	
133-3-1	Name of depositary institution	American Type Culture Collection
133-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
133-3-3	Date of deposit	14 April 1998 (14.04.1998)
133-3-4	Accession Number	ATCC 209772
133-4	Additional Indications	NONE
133-5	Designated States for Which Indications are Made	all designated States
133-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
134	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
134-1	page	101
134-2	line	21
134-3	Identification of Deposit	
134-3-1	Name of depositary institution	American Type Culture Collection
134-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
134-3-3	Date of deposit	16 October 1997 (16.10.1997)
134-3-4	Accession Number	ATCC 209375
134-4	Additional Indications	NONE
134-5	Designated States for Which Indications are Made	all designated States
134-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
135	the International Bureau later The indications made below relate to	
135	the deposited microorganism(s) or	•
	other biological material referred to in	
135-1	the description on: page	101
135-2	line	101
133-2	mid	22

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	Identification of Deposit	
135-3-1	Name of depositary institution	American Type Culture Collection
135-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
135-3-3	Date of deposit	23 September 1997 (23.09.1997)
135-3-4	Accession Number	ATCC 209296
135-4	Additional Indications	NONE
135-5	Designated States for Which	
	Indications are Made	all designated States
135-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
136	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
136-1	page	101
136-2	line	23
136-3	Identification of Deposit	
136-3-1	Name of depositary institution	American Type Culture Collection
136-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	·	America
136-3-3	Date of deposit	18 September 1997 (18.09.1997)
136-3-4	Accession Number	ATCC 209279
136-4	Additional Indications	NONE
136-5	Designated States for Which Indications are Made	all designated States
136-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
137	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
137-1	page	101
137-2	line	24
	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
137-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	05 March 1998 (05.03.1998)
		ATCC 209653
137-4	Additional Indications	NONE
137-5	Designated States for Which Indications are Made	all designated States
137-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	

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138	The indications made below relate to the deposited microorganism(s) or other biological material referred to in	
138-1	the description on:	101
138-2	line	125
138-3	Identification of Deposit	25
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
138-3-3	Date of deposit	16 October 1997 (16.10.1997)
138-3-4	Accession Number	ATCC 209385
138-4	Additional Indications	NONE
138-5	Designated States for Which	
	Indications are Made	all designated States
138-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
139	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
139-1	page	101
139-2	line	26
139-3	Identification of Deposit	
139-3-1	Name of depositary institution	American Type Culture Collection
139-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
139-3-3	Date of deposit	16 September 1997 (16.09.1997)
139-3-4	Accession Number	ATCC 209261
139-4	Additional Indications	NONE
139-5	Designated States for Which Indications are Made	all designated States
139-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
140	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	·
	the description on:	·
140-1	page 	101
	line	27
	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
140-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	Data of days 19	America
- 1	Date of deposit	16 October 1997 (16.10.1997)
	Accession Number	ATCC 209384
	Additional Indications	NONE
	Designated States for Which Indications are Made	all designated States

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140-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 141 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 141-1 page 101 141-2 28 141-3 Identification of Deposit 141-3-1 Name of depositary institution American Type Culture Collection 141-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 141-3-3 Date of deposit 16 September 1997 (16.09.1997) 141-3-4 Accession Number ATCC 209258 Additional Indications NONE **Designated States for Which** all designated States Indications are Made 141-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 142 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 142-1 page 101 142-2 line 29 142-3 Identification of Deposit 142-3-1 Name of depositary institution American Type Culture Collection 142-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 142-3-3 Date of deposit 16 September 1997 (16.09.1997) 142-3-4 Accession Number ATCC 209257 142-4 Additional Indications NONE 142-5 **Designated States for Which** all designated States Indications are Made 142-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 143 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 143-1 page 101 143-2 30 143-3 **Identification of Deposit** 143-3-1 Name of depositary institution American Type Culture Collection 143-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 143-3-3 Date of deposit 30 May 1997 (30.05.1997) 143-3-4 Accession Number

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143-4	Additional Indications	NONE
143-5	Designated States for Which	all designated States
440.0	Indications are Made	
143-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
144	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	<u> </u>
144-1	page	101
144-2	line	31
144-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
144-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
144-3-3	Date of deposit	16 October 1997 (16.10.1997)
144-3-4	Accession Number	ATCC 209381
144-4	Additional Indications	NONE
144-5	Designated States for Which Indications are Made	all designated States
144-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
145	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	·
145-1	page	101
145-2	line	32
145-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
145-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
145-3-3	Date of deposit	16 September 1997 (16.09.1997)
145-3-4	Accession Number	ATCC 209262
145-4	Additional Indications	NONE
145-5	Designated States for Which Indications are Made	all designated States
145-6		NONE
}	These indications will be submitted to	
	the International Bureau later	
146	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
146-1	page	101
146-2	line	33
140-2	ine .	33

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146-3	Identification of Deposit	T
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
	,	_ ,
		Virginia 20110-2209United States of
146.3.3	Date of deposit	America
	Accession Number	28 October 1997 (28.10.1997)
146-4		ATCC 209420
	Additional Indications	NONE
146-5	Designated States for Which Indications are Made	all designated States
146-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
147	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
147-1	page	101
147-2	line	34
147-3	Identification of Deposit	
147-3-1	Name of depositary institution	American Type Culture Collection
147-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
147-3-3	Date of deposit	16 September 1997 (16.09.1997)
147-3-4	Accession Number	ATCC 209256
147-4	Additional Indications	NONE
147-5	Designated States for Which Indications are Made	all designated States
147-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
148	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
148-1	page	101
148-2	fine	35
148-3	Identification of Deposit	
148-3-1	Name of depositary institution	American Type Culture Collection
148-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
148-3-3	Date of deposit	16 September 1997 (16.09.1997)
148-3-4	Accession Number	ATCC 209251
148-4	Additional Indications	NONE
148-5	Designated States for Which	all designated States
148-6	Indications are Made Separate Furnishing of Indications	
	These indications will be submitted to	NONE

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149	The indications made below relate to	T
	the deposited microorganism(s) or	
	other biological material referred to in	
440.4	the description on:	·
149-1	page	101
149-2	line	36
149-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
149-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
149-3-3	Date of deposit	16 September 1997 (16.09.1997)
149-3-4	Accession Number	ATCC 209263
149-4	Additional Indications	NONE
149-5	Designated States for Which	all designated States
110.0	Indications are Made	
149-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
150	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in	•
150-1	the description on:	101
150-2	line	101
150-2		37
	Identification of Deposit Name of depositary institution	la color de la col
i	Address of depositary institution	American Type Culture Collection
150-5-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	16 September 1997 (16.09.1997)
	Accession Number	ATCC 209264
150-4	Additional Indications	NONE
150-5	Designated States for Which Indications are Made	all designated States
150-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
151	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
151-1	page	101
151-2	line	38
151-3	Identification of Deposit	
151-3-1	Name of depositary institution	American Type Culture Collection
151-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	-	Virginia 20110-2209United States of
		America
151-3-3	Date of deposit	
	Accession Number	16 October 1997 (16.10.1997)
151-3-4		ATCC 209376
		NONE
151-5	Designated States for Which Indications are Made	all designated States

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151-6	Separate Furnishing of Indications	I
131-0	1	NONE
	These indications will be submitted to the International Bureau later	
152	The indications made below relate to	
	the deposited microorganism(s) or	· ·
	other biological material referred to in the description on:	
152-1	page	101
152-2	line	39
152-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
152-3-3	Date of deposit	1
	Accession Number	17 October 1997 (17.10.1997)
152-4	Additional Indications	ATCC 209391
152-5		NONE
104-0	Designated States for Which Indications are Made	all designated States
152-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
450	the International Bureau later	
153	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
452.4	the description on:	
153-1	page 	101
153-2	line	40
1 53-3 153-3-1	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
103-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
450 0 0		America
	Date of deposit	28 October 1997 (28.10.1997)
	Accession Number	ATCC 209417
153-4	Additional Indications	NONE
153-5	Designated States for Which Indications are Made	all designated States
153-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NORE
	the International Bureau later	•
154	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
154-1	page	101
154-2	line	41
154-3	Identification of Deposit	
		American Type Culture Collection
154-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	ĺ	Virginia 20110-2209United States of
		America
154-3-3	l 	16 September 1997 (16.09.1997)
154-3-4	la ,	ATCC 209253

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154-4	Additional Indications	NONE
154-5	Designated States for Which Indications are Made	all designated States
154-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
155	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
155-1	the description on:	
	page	101
155-2	line	42
155-3 155-3-1	Identification of Deposit Name of depositary institution	Dennison Charles Calledia
	Address of depositary institution	American Type Culture Collection
100-0-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
166 3 3	Date of deposit	America
	Accession Number	12 May 1998 (12.05.1998)
155-4	Additional Indications	ATCC 209855
		NONE
155-5	Designated States for Which Indications are Made	all designated States
155-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
156	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
156-1	page	101
156-2	line	43
156-3	Identification of Deposit	
156-3-1	Name of depositary institution	American Type Culture Collection
156-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
156-3-3	Date of deposit	10 December 1997 (10.12.1997)
156-3-4	Accession Number	ATCC 209526
156-4	Additional Indications	NONE
156-5	Designated States for Which Indications are Made	all designated States
156-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
157	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
157-1	page	101
157-2	line	44
	L	

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157-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
157-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	, ,	Virginia 20110-2209United States of
		America
157-3-3	Date of deposit	16 September 1997 (16.09.1997)
	Accession Number	· · · · · · · · · · · · · · · · · · ·
157-4	Additional Indications	ATCC 209252
157-5		NONE
157-5	Designated States for Which Indications are Made	all designated States
157-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
158	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
158-1	page	101
158-2	line	45
158-3	Identification of Deposit	
158-3-1	Name of depositary institution	American Type Culture Collection
158-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
58-3-3	Date of deposit	16 October 1997 (16.10.1997)
158-3-4	Accession Number	ATCC 209374
158-4	Additional Indications	NONE
158-5	Designated States for Which Indications are Made	all designated States
158-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
159	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	·
159-1	page	101
159-2	line	46
59-3	Identification of Deposit	
159-3-1	Name of depositary institution	American Type Culture Collection
159-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
59-3-3	Date of deposit	10 December 1997 (10.12.1997)
	Accession Number	ATCC 209528
159-4	Additional Indications	NONE
159-5	Designated States for Which	
. 55-5	Indications are Made	all designated States
159-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	

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160	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
160-1	page	101
160-2	line	47
160-3	Identification of Deposit	4/
160-3-1	1	American Type Culture Collection
160-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
160-3-3	Date of deposit	16 September 1997 (16.09.1997)
	Accession Number	ATCC 209265
160-4	Additional Indications	NONE
160-5	Designated States for Which	all designated States
	Indications are Made	all designated states
160-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
161	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
161-1	page	101
161-2	line	48
161-3	Identification of Deposit	
161-3-1	Name of depositary institution	American Type Culture Collection
161-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
161-3-3	Date of deposit	17 October 1997 (17.10.1997)
161-3-4	Accession Number	ATCC 209396
161-4	Additional Indications	NONE
161-5	Designated States for Which Indications are Made	all designated States
161-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
162	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
162-1	the description on:	101
162-2	line	101
162-3	Identification of Deposit	49
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
	, , , , , , , , , , , , , , , , , , , ,	Virginia 20110-2209United States of
		America
162-3-3	Date of deposit	18 August 1997 (18.08.1997)
	Accession Number	
162-4	Additional Indications	ATCC 209201
162-5	Designated States for Which	NONE
.02.0	Indications are Made	all designated States

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162-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
163	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
163-1	page	101
163-2	line	50
163-3	Identification of Deposit	
163-3-1	Name of depositary institution	American Type Culture Collection
163-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
163-3-3	Date of deposit	28 October 1997 (28.10.1997)
163-3-4	Accession Number	ATCC 209416
163-4	Additional Indications	NONE
163-5	Designated States for Which Indications are Made	all designated States
163-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
164	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
164-1	page	101
164-2	line	51
164-3	Identification of Deposit	
164-3-1	Name of depositary institution	American Type Culture Collection
164-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
164-3-3	Date of deposit	17 October 1997 (17.10.1997)
164-3-4	Accession Number	ATCC 209403
164-4	Additional Indications	NONE
164-5	Designated States for Which	all designated States
	Indications are Made	412 4001gillood 000000
164-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
165	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
165-1	page	101
165-2	line	52
165-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
165-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
165-3-3	Date of deposit	28 October 1997 (28.10.1997)
	Accession Number	ATCC 209419
		MICC 703413

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165-4	Additional Indications	NONE
165-5	Designated States for Which Indications are Made	all designated States
165-6	Separate Furnishing of Indications	NONE
_	These indications will be submitted to the International Bureau later	
166	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
166-1	page	101
166-2	line	53
166-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
166-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	17 October 1997 (17.10.1997)
	Accession Number	ATCC 209402
166-4	Additional Indications	NONE
166-5	Designated States for Which Indications are Made	all designated States
166-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
167	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
167-1	page	101
167-2	tine	54
167-3	Identification of Deposit	
167-3-1	Name of depositary institution	American Type Culture Collection
167-3-2	Address of depositary institution	10801 University Blvd., Manassas,
•		Virginia 20110-2209United States of
		America
167-3-3	Date of deposit	16 October 1997 (16.10.1997)
167-3-4	Accession Number	ATCC 209378
167-4	Additional Indications	NONE
167-5	Designated States for Which Indications are Made	all designated States
167-6	Separate Furnishing of Indications	NONE
_	These indications will be submitted to the International Bureau later	
168	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
168-1	page	101
168-2	line	55

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168-3	Identification of Deposit	
168-3-1	Name of depositary institution	American Type Culture Collection
168-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
168-3-3	Date of deposit	
	Accession Number	21 November 1997 (21.11.1997)
168-4	Additional Indications	ATCC 209489
168-5		NONE
	Designated States for Which Indications are Made	all designated States
168-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
169	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
169-1	page	102
169-2	line	2
169-3	Identification of Deposit	
	The state of the s	American Type Culture Collection
169-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
169-3-3	Date of deposit	17 October 1997 (17.10.1997)
169-3-4	Accession Number	ATCC 209401
169-4	Additional Indications	NONE
169-5	Designated States for Which Indications are Made	all designated States
169-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
170	the International Bureau later The indications made below relate to	
170	the deposited microorganism(s) or	
	other biological material referred to in	
170-1	the description on:	100
170-2	line	102
170-2	Identification of Deposit	3
	Name of depositary institution	Amorian Timo Culture Collection
	Address of depositary institution	American Type Culture Collection 10801 University Blvd., Manassas,
i	-	Virginia 20110-2209United States of
		America
170-3-3	Date of deposit	17 October 1997 (17.10.1997)
170-3-4	Accession Number	ATCC 209397
170-4	A 1 1241 A 1 11 41	NONE
170-5	Designated States for Which Indications are Made	all designated States
170-6	Concerts Franciski and the st	NOVE
	These indications will be submitted to	NONE
	the International Bureau later	

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171	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
171-1	page	102
171-2	line	4
171-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
171-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
474.0.0		America
	Date of deposit	17 October 1997 (17.10.1997)
171-3-4	Accession Number Additional Indications	ATCC 209389
171-5		NONE
	Designated States for Which Indications are Made	all designated States
171-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
172	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
172-1	page	102
172-2	line	5
172-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
172-3-2	Address of depositary institution	10801 University Blvd., Manassas,
]	Virginia 20110-2209United States of
172-3-3	Date of deposit	America
	Accession Number	07 November 1997 (07.11.1997)
172-4	A deliate and the second	ATCC 209438
172-5	Designated States for Which	NONE
	Indications are Made	all designated States
172-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
173	The Indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
173-1	page	102
173-2		6
	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
1/3-3-2		10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
472 2 2	Date of a large	America
	Date of deposit	21 November 1997 (21.11.1997)
	A 1 1101	ATCC 209492
	Dealers I have a second	NONE
	Designated States for Which Indications are Made	all designated States

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173-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
174	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
174-1	page	102
174-2	line	7
174-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
174-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	}	Virginia 20110-2209United States of
		America
174-3-3	Date of deposit	17 October 1997 (17.10.1997)
174-3-4	Accession Number	ATCC 209388
174-4	Additional Indications	NONE
174-5	Designated States for Which	all designated States
474.0	Indications are Made	ari designated states
174-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	· ·
175	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	,
175-1	page	102
175-2	line	8
175-3	Identification of Deposit	
175-3-1	Name of depositary institution	American Type Culture Collection
175-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
175-3-3	Date of deposit	07 November 1997 (07.11.1997)
175-3-4	Accession Number	ATCC 209432
175-4	Additional Indications	NONE
175-5	Designated States for Which	all designated States
	Indications are Made	all designated states
175-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
176	The indications made below relate to	
	the deposited microorganism(s) or	,
	other biological material referred to in the description on:	
176-1		102
176-2	line	9
176-3	Identification of Deposit	3
	Managara and also as the second	American Type Culture Collection
		10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		-
176-3-3	Data at access	America
	l	07 November 1997 (07.11.1997)
	- TOTO OF THE PROPERTY OF THE	ATCC 209439

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176-4	Additional Indications	NONE
176-5	Designated States for Which Indications are Made	all designated States
176-6	Separate Furnishing of Indications These indications will be submitted to	NONE
	the International Bureau later	
177	The indications made below relate to the deposited microorganism(s) or other biological material referred to in	
177-1	the description on:	100
177-2	line	102
177-3	Identification of Deposit	10
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
177-3-3	Date of deposit	07 November 1997 (07.11.1997)
177-3-4	Accession Number	ATCC 209433
177-4	Additional Indications	NONE
177-5	Designated States for Which	all designated States
177-6	Indications are Made Separate Furnishing of Indications	
•	These indications will be submitted to the International Bureau later	NONE
178	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	·
178-1	page	102
178-2	line	11
178-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
178-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	·	America
	Date of deposit	05 February 1998 (05.02.1998)
	Accession Number	ATCC 209618
178-4	Additional Indications	NONE
178-5	Designated States for Which Indications are Made	all designated States
178-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
179	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
179-1	page	102

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179-3	Identification of Deposit	
	Name of depositary institution	Smaniana Mara Cultura Callantia
	Address of depositary institution	American Type Culture Collection
173-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	_	America
	Date of deposit	21 November 1997 (21.11.1997)
179-3-4	Accession Number	ATCC 209484
179-4	Additional Indications	NONE
179-5	Designated States for Which Indications are Made	all designated States
179-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	·
180	the International Bureau later The indications made below relate to	
100	the deposited microorganism(s) or	
	other biological material referred to in	_
100 1	the description on:	
180-1	page	102
180-2	line	13
180-3 180-3-1	Identification of Deposit Name of depositary institution	
_	,	American Type Culture Collection
180-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
180-3-3	Date of deposit	21 November 1997 (21.11.1997)
180-3-4	Accession Number	ATCC 209487
180-4	Additional Indications	NONE
180-5	Designated States for Which Indications are Made	all designated States
180-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
181	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
181-1	page	102
181-2	line	14
181-3	Identification of Deposit	
		American Type Culture Collection
181-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	07 November 1997 (07.11.1997)
181-3-4	Accession Number	ATCC 209434
181-4	A Law Committee of the	NONE
181-5	B 1 1 101 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	all designated States
181-6	Company E 1 1 1 2 11 11	NONE
	These indications will be submitted to the International Bureau later	

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182	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
182-1	the description on:	
	page	102
182-2	line	15
182-3 182-3-1	Identification of Deposit Name of depositary institution	American Three Culture Collection
	Address of depositary institution	American Type Culture Collection
	, and the second of the second	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
182-3-3	Date of deposit	26 March 1998 (26.03.1998)
	Accession Number	ATCC 209704
182-4	Additional Indications	NONE
182-5	Designated States for Which	all designated States
400.0	Indications are Made	all designated states
182-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
183	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	·
,	the description on:	
183-1	page	102
183-2	line	16
83-3	Identification of Deposit	,
	Name of depositary institution	American Type Culture Collection
183-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	28 April 1998 (28.04.1998)
	Accession Number	ATCC 209808
183-4	Additional Indications	NONE
183-5	Designated States for Which Indications are Made	all designated States
83-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
184	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in	
84-1	the description on:	102
84-2	line	17
84-3	Identification of Deposit	± /
	Name of depositary institution	American Type Culture Collection
84-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	·	America
84-3-3	Date of deposit	06 May 1998 (06.05.1998)
84-3-4	Accession Number	ATCC 209847
84-4	Additional Indications	NONE
	Designated States for Which	all designated States
	Indications are Made	

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184-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
185	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
185-1	page	102
185-2	line	18
185-3	Identification of Deposit	
185-3-1	Name of depositary institution	American Type Culture Collection
185-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
185-3-3	Date of deposit	05 February 1998 (05.02.1998)
185-3-4	Accession Number	ATCC 209616
185-4	Additional Indications	NONE
185-5	Designated States for Which	all designated States
	Indications are Made	arr designated states
185-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
186	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
186-1	page	102
186-2	line	19
86-3	Identification of Deposit	
86-3-1	•	American Type Culture Collection
186-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
186-3-3	Date of deposit	05 February 1998 (05.02.1998)
	Accession Number	ATCC 209619
186-4	Additional Indications	NONE
186-5	Designated States for Which	
100-5	Indications are Made	all designated States
186-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
187	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
187-1	page	102
87-2	line	20
87-3	Identification of Deposit	20
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
·	, , , , , , , , , , , , , , , , , , , ,	Virginia 20110-2209United States of
		America
		America
187-3-3	Date of deposit	11 3 1000 /11 00 1000\
	Date of deposit Accession Number	11 August 1998 (11.08.1998) ATCC 203109

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187-4	Additional Indications	NONE
187-5	Designated States for Which Indications are Made	all designated States
187-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
188	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
188-1	the description on:	102
188-2	line	21
188-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
188-3-3	Date of deposit	31 March 1998 (31.03.1998)
188-3-4	Accession Number	ATCC 209715
188-4	Additional Indications	NONE
188-5	Designated States for Which Indications are Made	all designated States
188-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
189	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
189-1	page	102
189-2	line	22
189-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
189-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	11 March 1998 (11.03.1998)
	Accession Number	ATCC 209669
189-4	Additional Indications	NONE
189-5	Designated States for Which Indications are Made	all designated States
189-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
	page	102
190-2	line .	23

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190-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
190-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
190-3-3	Date of deposit	23 June 1998 (23.06.1998)
190-3-4	Accession Number	ATCC 203002
190-4	Additional Indications	NONE
190-5	Designated States for Which	all designated States
	Indications are Made	all designated states
190-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
191	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in	
191-1	the description on:	102
191-2	line	
191-3	Identification of Deposit	24
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	
	i	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
101 3 3	Date of deposit	America
	1	26 March 1998 (26.03.1998)
	Accession Number	ATCC 209705
191-4	Additional Indications	NONE
191-5	Designated States for Which Indications are Made	all designated States
191-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
192	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
192-1	10000	
	page	102
	line	102 25
192-3	line Identification of Deposit	25
192-3 192-3-1	line Identification of Deposit Name of depositary institution	25 American Type Culture Collection
192-3 192-3-1	line Identification of Deposit	American Type Culture Collection 10801 University Blvd., Manassas,
192-3 192-3-1	line Identification of Deposit Name of depositary institution	25 American Type Culture Collection
192-3 192-3-1 192-3-2	line Identification of Deposit Name of depositary institution Address of depositary institution	American Type Culture Collection 10801 University Blvd., Manassas,
192-3 192-3-1 192-3-2	line Identification of Deposit Name of depositary institution	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of
192-3 192-3-1 192-3-2 192-3-3	line Identification of Deposit Name of depositary institution Address of depositary institution	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America
192-3 192-3-1 192-3-2 192-3-3 192-3-4	line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 16 June 1998 (16.06.1998)
192-3 192-3-1 192-3-2 192-3-3 192-3-4 192-4	line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 16 June 1998 (16.06.1998) ATCC 209981 NONE
192-3 192-3-1 192-3-2 192-3-3 192-3-4 192-4	line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 16 June 1998 (16.06.1998) ATCC 209981 NONE all designated States
192-3 192-3-1 192-3-2 192-3-3 192-3-4 192-4 192-5	line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 16 June 1998 (16.06.1998) ATCC 209981 NONE

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193	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
193-1	page	102
193-2	line	26
193-3	Identification of Deposit	
193-3-1	Name of depositary institution	American Type Culture Collection
193-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
193-3-3	Date of deposit	07 April 1998 (07.04.1998)
193-3-4	Accession Number	ATCC 209749
193-4	Additional Indications	NONE
193-5	Designated States for Which	all designated States
193-6	Indications are Made Separate Furnishing of Indications	
133-0		NONE.
	These indications will be submitted to the International Bureau later	
194	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
194-1	the description on:	
194-1	line	102
194-2	Identification of Deposit	27
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
	, , , , , , , , , , , , , , , , , , , ,	Virginia 20110-2209United States of
		America
194-3-3	Date of deposit	12 May 1998 (12.05.1998)
	Accession Number	ATCC 209859
194-4	Additional Indications	NONE
194-5	Designated States for Which	
	Indications are Made	all designated States
194-6	Separate Furnishing of Indications	NONE .
	These indications will be submitted to	
195	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
195-1	page	102
195-2	line	28
195-3	Identification of Deposit	
195-3-1	Name of depositary institution	American Type Culture Collection
195-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
95-3-3	Date of deposit	06 May 1998 (06.05.1998)
95-3-4	Accession Number	ATCC 209845
195-4	A 4 1141 A 4 11 A	NONE
95-5	Designated States for Which	all designated States
	Indications are Made	

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Separate Furnishing of Indications

These indications will be submitted to the International Bureau later

The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:

195-6

196

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NONE

106 4	nage	1.00
196-1	page	102
196-2	line	29
196-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
196-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
196-3-3	Date of deposit	07 April 1998 (07.04.1998)
196-3-4	Accession Number	ATCC 209748
196-4	Additional Indications	NONE
196-5	Designated States for Which	all designated States
	Indications are Made	dir designated blaces
196-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
197	the International Bureau later The indications made below relate to	·
	the deposited microorganism(s) or	
	other biological material referred to in	
197-1	the description on:	
197-2	[· ·	102
	line	30
97-3	Identification of Deposit Name of depositary institution	<u> </u>
	Address of depositary institution	American Type Culture Collection
197-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	11 August 1998 (11.08.1998)
	Accession Number	ATCC 203107
197-4	Additional Indications	NONE
197-5	Designated States for Which Indications are Made	all designated States
197-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
98	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	•
	the description on:	
98-1	page	102
98-2	line	31
	Identification of Deposit	
98-3-1	Name of depositary institution	American Type Culture Collection
98-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
98-3-3	Date of deposit	23 April 1998 (23.04.1998)
	Accession Number	-
		ATCC 209801

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198-4	Additional Indications	NONE
198-5	Designated States for Which Indications are Made	all designated States
198-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
199	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
199-1	page	102
199-2	line	32
199-3	Identification of Deposit	
199-3-1	Name of depositary institution	American Type Culture Collection
199-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
199-3-3	Date of deposit	09 June 1998 (09.06.1998)
199-3-4	Accession Number	ATCC 209948
199-4	Additional Indications	NONE
199-5	Designated States for Which Indications are Made	all designated States
199-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
200	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
200-1	page	102
200-2	line	33
200-3	Identification of Deposit	
200-3-1	Name of depositary institution	American Type Culture Collection
200-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
200-3-3	Date of deposit	20 May 1998 (20.05.1998)
200-3-4	Accession Number	ATCC 209883
200-4	Additional Indications	NONE
200-5	Designated States for Which Indications are Made	all designated States
200-6	Separate Furnishing of Indications	NONE
•	These indications will be submitted to the International Bureau later	
201	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
201-1	page	102
201-2	line	34

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201-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
201-3-3	Date of deposit	01 July 1998 (01.07.1998)
	Accession Number	ATCC 203049
201-4	Additional Indications	NONE
201-5	Designated States for Which	all designated States
	Indications are Made	all designated states
201-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
202	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	·
202-1	page	102
202-2	line	35
202-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
202-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	06 May 1998 (06.05.1998)
	Accession Number	ATCC 209846
202-4	Additional Indications	NONE
202-5	Designated States for Which Indications are Made	all designated States
202-6	Separate Furnishing of Indications	NONE
-	These indications will be submitted to the International Bureau later	
203	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
203-1	the description on: page	100
203-2	line	102
203-3	Identification of Deposit	36
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
203-3-3	Date of deposit	12 May 1998 (12.05.1998)
203-3-4	Accession Number	ATCC 209857
203-4	Additional Indications	NONE
203-5	Designated States for Which	all designated States
	Indications are Made	
203-6	Separate Furnishing of Indications	NONE
İ	These indications will be submitted to the International Bureau later	
		<u></u>

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204	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
204-1	page	102
204-2	line	37
204-3	Identification of Deposit	
204-3-1	Name of depositary institution	American Type Culture Collection
204-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
204-3-3	Date of deposit	14 May 1998 (14.05.1998)
204-3-4	Accession Number	ATCC 209864
204-4	Additional Indications	NONE
204-5	Designated States for Which	all designated States
204-6	Indications are Made	
204-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
205	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
205-1	page	102
205-2	line	138
205-3	Identification of Deposit	
205-3-1	Name of depositary institution	American Type Culture Collection
205-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
205-3-3	Date of deposit	20 May 1998 (20.05.1998)
205-3-4	Accession Number	ATCC 209880
205-4	Additional Indications	NONE
205-5	Designated States for Which	all designated States
205-6	Indications are Made Separate Furnishing of Indications	<u> </u>
205-0	These indications will be submitted to	NONE
	the International Bureau later	
206	The indications made below relate to	· · · · · · · · · · · · · · · · · · ·
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
206-1	page	102
206-2	line	39
206-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
206-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
206-3-3	Date of deposit	14 May 1998 (14.05.1998)
206-3-4	Accession Number	ATCC 209869
206-4	Additional Indications	NONE
206-5	Designated States for Which	all designated States
	Indications are Made	•

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206-6	Separate Furnishing of Indications	[5-23
200-0	ļ '	NONE
	These indications will be submitted to the International Bureau later	
207	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
207-1	page	102
207-2	line	40
207-3	Identification of Deposit	40
	Name of depositary institution	American Type Culture Collection
207-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Virginia 20110-2209United States of
		1 -
207-3-3	Date of deposit	America
	· '	09 June 1998 (09.06.1998)
	Accession Number	ATCC 209950
207-4	Additional Indications	NONE
207-5	Designated States for Which Indications are Made	all designated States
207-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
208	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
208-1	page	102
208-2	line	41
208-3	Identification of Deposit	
208-3-1	Name of depositary institution	American Type Culture Collection
208-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
208-3-3	Date of deposit	23 June 1998 (23.06.1998)
208-3-4	Accession Number	ATCC 203008
208-4	Additional Indications	NONE
208-5	Designated States for Which	all designated States
	Indications are Made	
208-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
209	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
209-1	page	102
209-2	line	42
209-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
209-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
209-3-3	Date of deposit	23 June 1998 (23.06.1998)
209-3-4	Accession Number	ATCC 203014
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209-4	Additional Indications	NONE
209-5	Designated States for Which Indications are Made	all designated States
209-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
210	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
210-1	page	102
210-2	line	43
210-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
210-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
210-3-3	Date of deposit	11 August 1998 (11.08.1998)
210-3-4	Accession Number	ATCC 203110
210-4	Additional Indications	NONE
210-5	Designated States for Which Indications are Made	all designated States
210-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
211	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
211-1	page	102
211-2	line	44
211-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
211-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	İ	America
1	Date of deposit	23 June 1998 (23.06.1998)
	Accession Number	ATCC 203009
211-4		NONE
	mulcations are made	all designated States
211-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
212-1	page	102

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212-3	Identification of Deposit	
212-3-1	Name of depositary institution	American Type Culture Collection
212-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	į.	America
212-3-3	Date of deposit	09 June 1998 (09.06.1998)
	Accession Number	·
212-4	Additional Indications	ATCC 209961
212-5	Designated States for Which	NONE
	Indications are Made	all designated States
212-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
213	The Indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	· ·
	the description on:	
213-1	page	102
213-2	line	46
213-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
213-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
213-3-3	Date of deposit	09 June 1998 (09.06.1998)
213-3-4	Accession Number	ATCC 209962
213-4	Additional Indications	NONE
213-5	Designated States for Which Indications are Made	all designated States
213-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
214	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
	the description on:	
	page	102
	line	47 -
14-3	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
. 17-3-4	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
.,, .,	Data of dance!	America
	Date of deposit	14 May 1998 (14.05.1998)
		ATCC 209866
		NONE
	indications are made	all designated States
		NONE
	These indications will be submitted to the International Bureau later	

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the deposited microorganism(s) or other biological material referred to in the description on: 102 15-2 16-2 16-2 16-2 16-3	215	The indications made below relate to	T
102 103		the deposited microorganism(s) or	
215-2 Jage 102 48			
Identification of Deposit American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 25 August 1998 (25.08.1998) ATCC 203157 Additional Indications NONE August 1998 (25.08.1998) ATCC 203157 Additional Indications NONE August 1998 (25.08.1998) ATCC 203157 Additional Indications NONE August 1998 (25.08.1998) ATCC 203157 Additional Indications NONE August 1998 (25.08.1998) ATCC 203157 Additional Indications are Made August 1998 (25.08.1998) ATCC 203157 Additional Indications are Made August 1998 (25.08.1998) ATCC 203157 Additional Indications are Made August 1998 (25.08.1998) ATCC 203157 Additional Indications are Made August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 203106 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 August 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUGust 1998 (25.08.1998) ATCC 209945 AUgust 1998 (25.08.1998) ATCC 209	215-1	,	102
215-3-1 Name of depositary institution 215-3-2 Address of depositary institution 215-3-2 Address of depositary institution 215-3-3 Date of deposit 215-3-3 Date of deposit 215-3-4 Accession Number 215-4 Additional Indications 215-5 Designated States for Which Indications and Made Despoit Designated States for Which Indications are supported by the depositary institution 216-1 Designated States for Which Indications and Made Designated States for Which Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are supported by the Indications are Indicat	215-2	line	
215-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 25 August 1998 (25.08.1998) ATCC 203157 Additional Indications ATCC 203157 Additional Indications remade Additional Indications remade Additional Indications remade Additional Indications remade Additional Indications remade Additional Indications remade Additional Indications remade Additional Indications remains Address of depositary institution Address of depositary institution Address of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ATCC 203106 Additional Indications ATCC 203106 Additional Indications Address of depositary institution Address of depositary institution Address of depositary institution ATCC 203106 Additional Indications ATCC 203106 Additional Indications ATCC 203106 Additional Indications ATCC 203106 Additional Indications ATCC 203106 Additional Indications Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution American Type Culture Collection American Type Culture Co		Identification of Deposit	
215-3-2 Address of deposits 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 25 August 1998 (25.08.1998) ATCC 203157	215-3-1	Name of depositary institution	American Type Culture Collection
Virginia 20110-2209United States of America 215-3-3 Date of deposit 25 August 1998 (25.08.1998) 215-3-4 Accession Number ATCC 203157 215-4 Additional Indications are Made Indications Indica	215-3-2	Address of depositary institution	
Date of deposit 25 August 1998 (25.08.1998) ATCC 203157			
215-3-4 Accession Number ATCC 203157 215-3-4 Accession Number ATCC 203157 215-5 Designated States for Which Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications are Made Indications Indication			
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215-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications are Made 216-1 The indications and below relate to the Internations and part of the description on: page 102 216-1 Iline 49 216-3 Identification of Deposit 163-3 Date of deposit on the description on: page 11-2 Designated States for Which Indications and page 11-2 Designated States for Which Indications and page 11-2 Designated States for Which Indications and page 11-2 Designated States for Which Indications and page 11-2 Designated States for Which Indications and page 10-2 Designated States for Which Indications and page 10-2 Designated States for Which Indications and page 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications are Made 10-2 Designated States for Which Indications Indicat	215-3-4	Accession Number	
Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later 102	215-4	Additional Indications	NONE
215-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 216 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 216-1 Jine 49 216-2 line 49 216-3-1 Identification of Deposit Name of depositary institution 216-3-2 Address of depositary institution 216-3-3 Date of deposit 216-3-4 Accession Number Additional Indications 216-3-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217-1 Inne 217-1 Inne 217-1 Inne 217-2 Inne 217-3 Date of deposit 217-3-3 Date of deposit Order of the deposited microorganism(s) or other biological material referred to in the description on: 217-3 Date of deposit Order of the deposited microorganism(s) or other biological material referred to in the description on: 217-1 Page 102 217-3 Identification of Deposit Name of depositary institution Order of Deposit Name of depositary institution Order of Deposit Name of depositary institution Order of Deposit Name of depositary institution Order of Deposit Name of Deposit N	215-5		all designated States
These indications will be submitted to the International Bureau later 1016	215-6		
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other biological material referred to in the description on: page 102 216-2 line 49 216-3 line 49 216-3-1 Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) Accession Number Additional Indications These indications are Made 1909-1914 (1909-1914) 217-2 line 50 217-3-1 Sage 106-1914 (1909-1914) 217-3 lidentification of Deposit 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ATCC 203106 NONE 20110-2209United States of NONE 20110-20	216	The indications made below relate to	
the description on: page 102 216-2 216-3 line 49 216-3-1 216-3-1 216-3-3 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ACCESSION Number ATCC 203106 216-3 Additional indications NONE 11-6 Separate Furnishing of Indications These indications will be submitted to the international Bureau later 11-7-1 in edescription on: page 102 217-3 Identification of Deposit 217-3-1 Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ATCC 203106 NONE 11-6 Separate Furnishing of Indications These indications are Made to the international Bureau later 11-6 deposited microorganism(s) or other biological material referred to in the description on: page 102 217-3 Identification of Deposit 217-3-1 Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) ATCC 209945 217-4 Additional Indications NONE 217-5 Designated States for Which 211-6 designated States of States for Which 211-6 designated States States of World 211-6 designated States States States States of World 211-6 designated States St		the deposited microorganism(s) or other biological material referred to in	
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American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ATCC 203106 NONE 16-3 Designated States for Which Indications are Made 216-5 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 17 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 102 17-3 Identification of Deposit Name of depositary institution Address of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) 217-3 Accession Number 217-4 Additional Indications NONE	216-2	line	49
Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 11 August 1998 (11.08.1998) ATCC 203106 216-3 Accession Number 216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-3 Identification of Deposit Name of depositary institution Address of depositary institution Address of depositary institution America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE		Identification of Deposit	
Virginia 20110-2209United States of America 216-3-3 Date of deposit 216-3-4 Accession Number 216-4 Additional Indications 216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-2 line 217-3 Identification of Deposit Name of depositary institution Address of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE		T control of the cont	
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216-3-3 Date of deposit 216-3-4 Accession Number 216-4 Additional Indications 216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-2 line 217-3 Identification of Deposit 217-3-1 Address of depositary institution 217-3-2 Address of deposit 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications 217-5 Designated States for Which 218-1 Address of Which 219-8 (11.08.1998) ATCC 203106 210-8.1998) ATCC 203106 210-8.1998) ATCC 203106 210-8.1998) ATCC 203106 211.08.1998) ATCC 203106 212-3-4 Additional Indications 213-4 Additional Indications 214-4 Additional Indications 215-5 Designated States for Which 217-6 Leaves and English			Virginia 20110-2209United States of
216-3-4 Additional Indications 216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-2 line 217-3 Identification of Deposit 217-3-1 Name of depositary institution 217-3-2 Address of depositary institution 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE NONE NONE 102 102 102 102 103 104 105 105 107 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 109 June 1998 (09.06.1998) ATCC 209945 NONE	046 0 0		
216-4 Additional Indications 216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 217-1 page 217-2 line 217-3 Identification of Deposit Name of depositary institution 217-3-2 Address of depositary institution 217-3-2 Date of deposit 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE NONE NONE			11 August 1998 (11.08.1998)
216-5 Designated States for Which Indications are Made 216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-2 line 217-3 Identification of Deposit Name of depositary institution 217-3-2 Address of depositary institution 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE		<u> </u>	
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216-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 217 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 217-1 page 217-2 line 217-3 Identification of Deposit Name of depositary institution 217-3-1 Address of depositary institution 217-3-2 Date of deposit 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE NONE	216-5		all designated States
These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page line 102 217-2 line 50 217-3-1 Identification of Deposit Name of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 217-3-3 Date of deposit Openation Op	216-6		NONE
The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 217-1 page 217-2 line 217-3 Identification of Deposit Name of depositary institution Address of depositary institution Address of depositary institution Date of deposit 217-3-4 Accession Number 217-4 Additional Indications Designated States for Which Topic Indications made below relate to the deposit or other biological material to the deposit or other biological material referred to in the deposit or other biological material referred to in the description on: 102 50 American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) ATCC 209945		These indications will be submitted to	•10•12
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other biological material referred to in the description on: page line 217-1 217-2 line 217-3 lidentification of Deposit Name of depositary institution 217-3-1 217-3-2 Date of deposit 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications Designated States for Which 217-5 Designated States for Which 217-1 217-	217	the deposited microgramism(s) or	
217-1 page 102 50 217-3 Identification of Deposit Name of depositary institution Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America O9 June 1998 (09.06.1998) ATCC 209945 Additional Indications NONE 217-5 Designated States for Which 211 designated States Control of the page Con		other biological material referred to in	
217-2 line 50 217-3 Identification of Deposit Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 217-3-3 Date of deposit 09 June 1998 (09.06.1998) 217-3-4 Accession Number ATCC 209945 217-5 Designated States for Which 217-5 Designated States for Which 217-6 Designated States for Which 217-8 Designated States for Which	217-1		•••
217-3 Identification of Deposit 217-3-1 Name of depositary institution 217-3-2 Address of depositary institution Address of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) 217-3-4 Accession Number ATCC 209945 NONE 217-5 Designated States for Which 217-5 Designated States for Which 217-8 Additional Indications 217-8 Additional Indications 218-8 Additional Indications 218-8 Additional Indications 219-8 Additional Indica		l' *	
217-3-1 Name of depositary institution 217-3-2 Address of depositary institution American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) 217-3-4 Accession Number 217-4 Additional Indications NONE 217-5 Designated States for Which 217-6 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of American Type Culture Collection			50
Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications NONE 217-5 Designated States for Which 217-5 Designated States for Which 217-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 June 1998 (09.06.1998) ATCC 209945	-	Name of description of	Amorican Shows Culture Callastics
Virginia 20110-2209United States of America 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications 217-5 Designated States for Which 217-5 Designated States for Which 217-6 Posignated States for Which 218-6 Posignated States for Which 218-6 Posignated States for Which 218-7 Posignated States for Which 218-7 Posignated States for Which 218-7 Posignated States for Which 219-7 Posignated St		-	
America 217-3-3 Date of deposit 217-3-4 Accession Number 217-4 Additional Indications 217-5 Designated States for Which 217-5 Designated States for Which 217-5 Date of deposit 217-6 Open 1998 (09.06.1998) 217-7 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which 217-8 Designated States for Which			
217-3-3 Date of deposit 09 June 1998 (09.06.1998) 217-3-4 Accession Number ATCC 209945 217-4 Additional Indications NONE 217-5 Designated States for Which all designated States			-
217-3-4 Accession Number ATCC 209945 217-4 Additional Indications NONE 217-5 Designated States for Which all designated States	217-3-3	- · · · · · · · · · · · · · · · · · · ·	
217-4 Additional Indications NONE 217-5 Designated States for Which all designated States		Annania Alumba	
217-5 Designated States for Which all designated States		A deltate 1 to - 41	
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			all designated States

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217-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
218	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
040.4	the description on:	
218-1	page	102
218-2	line	51
218-3 218-3-1	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
210-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
210 2 2	Data of danceit	America
	Date of deposit	16 June 1998 (16.06.1998)
218-3-4		ATCC 209989
218-4	Additional Indications	NONE
218-5	Designated States for Which Indications are Made	all designated States
218-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
219	the International Bureau later The indications made below relate to	
	the deposited microorganism(s) or	·
	other biological material referred to in the description on:	
219-1	page	102
219-2	line	52
219-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
219-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	11 August 1998 (11.08.1998)
	Accession Number	ATCC 203108
219-4	Additional Indications	NONE
219-5	Designated States for Which	all designated States
219-6	Indications are Made Separate Furnishing of Indications	MANTE
	These indications will be submitted to	NONE
	the International Bureau later	
220	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
220-1	page	102
220-2	line	53
220-3	Identification of Deposit	
220-3-1	,	American Type Culture Collection
220-3-2	Address of depositary institution	10801 University Blvd., Manassas,
•		Virginia 20110-2209United States of
	i i	America
	Date of deposit	11 August 1998 (11.08.1998)
220-3-4	Accession Number	ATCC 203111

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220-4	Additional Indications	NONE
220-5	Designated States for Which Indications are Made	all designated States
220-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
221	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
221-1	page	102
221-2	line	54
221-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
221-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
221 -3 -3	Date of deposit	20 October 1998 (20.10.1998)
221-3-4	Accession Number	ATCC 203359
221-4	Additional Indications	NONE
221-5	Designated States for Which Indications are Made	all designated States
221-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
222	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
222-1	page	102
222-2	line	55
222-3	Identification of Deposit	
222-3-1	Name of depositary institution	American Type Culture Collection
222-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
222-3-3	Date of deposit	16 June 1998 (16.06.1998)
22-3-4	Accession Number	ATCC 209988
222-4	Additional Indications	NONE
222-5	Designated States for Which Indications are Made	all designated States
222-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
223	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
223-1	page	103

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		Identification of Deposit
	American Type Culture Collection	Name of depositary institution
	10801 University Blvd., Manassas,	Address of depositary institution
Ē	Virginia 20110-2209United States of	
-	America	
	16 June 1998 (16.06.1998)	Date of deposit
	ATCC 209978	Accession Number
	NONE	Additional Indications
	all designated States	Designated States for Which
		Indications are Made
	NONE	Separate Furnishing of Indications
		These indications will be submitted to the International Bureau later
		The indications made below relate to
		the deposited microorganism(s) or other biological material referred to in
		the description on:
	103	page
	3	line
		Identification of Deposit
	American Type Culture Collection	Name of depositary institution
	10801 University Blvd., Manassas,	Address of depositary institution
Ē	Virginia 20110-2209United States of	
	America	
	04 August 1998 (04.08.1998)	Date of deposit
	ATCC 203098	Accession Number
	NONE	Additional Indications
	all designated States	Designated States for Which Indications are Made
	NONE	Separate Furnishing of Indications
		These indications will be submitted to the International Bureau later
		The indications made below relate to the deposited microorganism(s) or
		other biological material referred to in
		the description on:
		•
	4	
	American Tune Culture Collection	Name of depositary institution
		Address of depositary institution
=		•
•		
		Date of deposit
		Accession Number
		Additional Indications
		Designated States for Which
		Indications are Made
	NONE	· . •
		These indications will be submitted to
	American Type Culture Collection 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 16 June 1998 (16.06.1998) ATCC 209980 NONE all designated States	page line Identification of Deposit Name of depositary institution Address of depositary institution Date of deposit Accession Number Additional Indications Designated States for Which Indications are Made Separate Furnishing of Indications

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226	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
226-1	page	103
226-2	line	5
	Identification of Deposit	
26-3-1	Name of depositary institution	American Type Culture Collection
226-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
226-3-3	Date of deposit	04 August 1998 (04.08.1998)
226-3-4	Accession Number	ATCC 203091
226-4	Additional Indications	NONE
226-5	Designated States for Which	
.20-0	Indications are Made	all designated States
226-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
227	the International Bureau later The indications made below relate to	
221	the deposited microorganism(s) or	
	other biological material referred to in	
207.4	the description on:	
227-1	page	103
227-2	line	6
227-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
227-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	:	Virginia 20110-2209United States of
		America
227-3-3	Date of deposit	04 August 1998 (04.08.1998)
227-3-4	Accession Number	ATCC 203090
227-4	Additional Indications	NONE
227-5	Designated States for Which	all designated States
227-6	Indications are Made Separate Furnishing of Indications	YOUR
	These indications will be submitted to	NONE
	the International Bureau later	
228	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
228-1	page	103
228-2	line	7
228-3	Identification of Deposit	
228-3-1	Name of depositary institution	American Type Culture Collection
228-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
228-3-3	Date of deposit	
	Accession Number	04 August 1998 (04.08.1998)
		ATCC 203092
228-4 228-5	Additional Indications	NONE
	Designated States for Which	all designated States

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228-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONZ
	the International Bureau later	
229	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
229-1	page	103
229-2	line	8
229-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
229-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
229-3-3	Date of deposit	10 November 1998 (10.11.1998)
229-3-4	Accession Number	ATCC 203452
229-4	Additional Indications	NONE
229-5	Designated States for Which Indications are Made	all designated States
229-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
230	the International Bureau later The indications made below relate to	
250	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
230-1	page	103
230-2	line	9
230-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
230-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
230-3-3	Date of deposit	01 September 1998 (01.09.1998)
230-3-4	Accession Number	ATCC 203173
230-4	Additional Indications	NONE
230-5	Designated States for Which	all designated States
230-6	Indications are Made Separate Furnishing of Indications	NOME
	These indications will be submitted to	NONE
	the International Bureau later	
231	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
•	the description on:	
231-1	page	103
231-2	line	10
231-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
231-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
231-3-3	Date of deposit	17 November 1998 (17.11.1998)
231-3-4	Accession Number	ATCC 203464

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231-4	Additional Indications	NONE
231-5	Designated States for Which Indications are Made	all designated States
231-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
232	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
232-1	page	103
232-2	line	11
	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
232-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	18 August 1998 (18.08.1998)
	Accession Number	ATCC 203132
232-4	Additional Indications	NONE
232-5	Designated States for Which Indications are Made	all designated States
232-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
233	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
233-1	page	103
233-2	line	12
233-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
233-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	09 September 1998 (09.09.1998)
	Accession Number	ATCC 203254
233-4	Additional Indications	NONE
233-5	Designated States for Which Indications are Made	all designated States
233-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
234	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
234-1	page	103
234-2	line	13
		<u> </u>

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234-3	Identification of Denset	
	Identification of Deposit Name of depositary institution	Amonican Ermo Cultura Callestian
	Address of depositary institution	American Type Culture Collection
234-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
234-3-3	Date of deposit	America
	Accession Number	20 October 1998 (20.10.1998)
234-3-4	Additional Indications	ATCC 203358
		NONE
234-5	Designated States for Which Indications are Made	all designated States
234-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
235	the International Bureau later The indications made below relate to	
200	the deposited microorganism(s) or	
	other biological material referred to in	
235-1	the description on:	103
235-2	line	114
235-3	Identification of Deposit	1.4
	Name of depositary institution	American Type Culture Collection
235-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	-	Virginia 20110-2209United States of
		America
235-3-3	Date of deposit	04 August 1998 (04.08.1998)
	Accession Number	ATCC 203093
235-4	Additional Indications	NONE
235-5	Designated States for Which	all designated States
	Indications are Made	all designated states
235-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	,
236	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
	the description on:	
236-1	page	103
236-2	line	15
236-3	Identification of Deposit	
236-3-1	,	American Type Culture Collection
236-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	03 November 1998 (03.11.1998)
236-3-4	Accession Number	ATCC 203457
236-4	Additional Indications	NONE
236-5	Designated States for Which	all designated States
236-6	Indications are Made Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	

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237	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
237-1	page	103
237-2	line	16
237-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
	, ,	Virginia 20110-2209United States of
		America
237-3-3	Date of deposit	09 September 1998 (09.09.1998)
	Accession Number	ATCC 203241
237-4	Additional Indications	NONE
237-5	Designated States for Which	all designated States
	Indications are Made	arr designated states
237-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
238	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
238-1	page	103
238-2	line	17
238-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
238-3-2	Address of depositary institution	10801 University Blvd., Manassas,
i		Virginia 20110-2209United States of
		America
238-3-3	Date of deposit	09 September 1998 (09.09.1998)
238-3-4	Accession Number	ATCC 203249
238-4	Additional Indications	NONE
238-5	Designated States for Which Indications are Made	all designated States
238-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	******
	the International Bureau later	
239	The indications made below relate to the deposited microorganism(s) or	·
	other biological material referred to in	
239-1	the description on:	
	page	103
239-2	line	18
239-3 239-3-1	Identification of Deposit Name of depositary institution	Amorican Type Culture Callection
	Address of depositary institution	American Type Culture Collection
• -	The state of the s	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
230-3-3	Date of deposit	America
	Accession Number	09 September 1998 (09.09.1998)
239-3-4	Additional Indications	ATCC 203250
239-4 239-5		NONE
£35-3	Designated States for Which Indications are Made	all designated States

242-3-4 Accession Number

P3330R1 Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM 239-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 240 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 240-1 page 103 240-2 line 19 240-3 Identification of Deposit 240-3-1 Name of depositary institution American Type Culture Collection 240-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 240-3-3 Date of deposit 18 August 1998 (18.08.1998) 240-3-4 **Accession Number** ATCC 203131 240-4 **Additional Indications** NONE 240-5 **Designated States for Which** all designated States Indications are Made 240-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 241-1 103 241-2 20 241-3 **Identification of Deposit** 241-3-1 Name of depositary institution American Type Culture Collection 241-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 241-3-3 Date of deposit 15 September 1998 (15.09.1998) 241-3-4 Accession Number ATCC 203223 241-4 Additional Indications NONE **Designated States for Which** all designated States Indications are Made 241-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 242 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 242-1 page 103 242-2 line 21 Identification of Deposit 242-3 Name of depositary institution American Type Culture Collection Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 242-3-3 Date of deposit 15 September 1998 (15.09.1998)

ATCC 203233

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Designated States for Which Indications are Made Separate Furnishing of Indications NONE	242-4	Additional Indications	NONE
These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 243-1 page 103 243-2 line 22 243-3 Identification of Deposit Address of depositary institution Address of depositary institution Address of depositary institution Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 September 1998 (09.09.1998) ATCC 203252 Additional Indications NONE Additional Indications NONE Additional Indications will be submitted to the International Bureau later The Indications and below relate to the deposited microorganism(s) or other biological material referred to in the description on: 244-3 Date of deposit 103 Date of deposit 23 Date of depositary institution These indications of Deposit 103 Address of depositary institution 23 Address of depositary institution 244-3. Identification of Deposit 103 Address of depositary institution 244-3. Identification of Deposit 103 Address of depositary institution 244-3. Identification of Deposit 103 Address of depositary institution 244-3. Identification of Deposit 103 Address of depositary institution 244-3. Identification of Deposit 103 Accession Number 244-4 Address on Number 244-4 Address on Number 244-4 Address on Number 244-4 Address on Number 244-4 Address on Number 244-4 Address on Number 244-5 Designated States for Which indications are Made to the International Bureau later 100 The description on: 044-4 Address on Number 104-4 242-5	, ,	all designated States	
the International Bureau later 143 The Indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 243-1 Jane of depositary institution 243-2 Jane of depositary institution 243-3-1 Address of depositary institution 243-3-3 Date of deposit 243-3-3 Date of deposit 243-4 Additional indications 243-5 Designated States for Which Indications are Made 244-5 Designated States for Which Indications are Made 244-1 page 103 244-3-1 Name of depositary institution 244-3-1 Name of depositary institution 244-3-3 Date of deposit 244-4 Additional indications 244-4 Accession Number 245-6 Separats Furnishing of Indications none the description on: 246-1 Designated States for Which Indications are Made 247-1 Page 103 103 103 103 104 105 105 107 108 108 109 109 109 109 109 109	242-6	Separate Furnishing of Indications	NONE
the deposited microorganism(s) or other biological material referred to in the description on: 243-1 page 103 243-2 line 22 243-3 lidentification of Deposit Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 September 1998 (09.09.1998) 243-3-4 Accession Number ATCC 203252 243-4 Additional Indications NONE 143-6 Separate Furnishing of Indications These indications are Made 154-2 line 23 244-3-1 line 23 244-3-1 line 23 244-3-1 lossification of Deposit NONE 103 244-3-1 lossification of Deposit NONE 103 244-3-2 Additional Indications NONE 103 244-3-1 lossification of Deposit None 104-1 lossification of Deposit None 104-1 lossification of Deposit None 105-1 lossification of Deposit None 105-1 lossification of Deposit None 105-1 lossification No			
other biological material referred to in the description on: 43-3-1 page 43-3-2 line 43-3-3-1 Name of depositary institution 43-3-3-2 Address of depositary institution 43-3-3-2 Address of depositary institution 43-3-3-4 Accession Number 43-3-3-4 Accession Number 43-3-5 Designated States for Which indications are Made 43-6 Separate Furnishing of Indications 43-6 The indications and be below relate to the deposited micrographism(s) or other biological material referred to in the description on: 43-1 Name of depositary institution 43-2 Address of depositary institution 43-3 Date of deposit in the description of Deposit 43-3-1 Date of deposit in the description of Deposit 43-3-1 Date of deposit in the description of Deposit 43-3-2 Address of depositary institution 43-4-3-2 Address of depositary institution 43-4-3-4 Accession Number 44-4-3-5 Designated States for Which indications are Made 44-3-1 Date of deposit in the description of Deposit 44-3-4 Accession Number 44-4-3-5 Designated States for Which indications are Made 44-4 Additional Indications 44-4 Additional Indications 44-5 Designated States for Which indications are Made 44-6 Separate Furnishing of Indications These indications will be submitted to the International Bursal later 44-6 Separate Furnishing of Indications These indications will be submitted to the International Bursal later 44-7 The Indications are Made 44-8 Separate Furnishing of Indications These indications will be submitted to the International Bursal later 44-8 The Indications are Made 44-9 The Indications are Made 44-1 The Indications are Made 44-2 The Indications are Made 44-3 The Indications are Made 44-4 Additional Indications 44-5 Designated States for Which indications are Made 44-6 The Indications are Made 44-7 The Indications are Made 44-8 The Indications are Made 44-9 The Indications are Made 44-1 The Indications are Made 44-1 The Indications are Made 44-1 The Indications are Made 44-1 The Indications are Made 44-2 The Indications ar	243		
the description on: page 103 243-2 line 222 243-3 lidentification of Deposit Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 09 September 1998 (09.09.1998) ATCC 203252 243-3 Additional Indications NONE 31 description on: These indications are Made 103 244-3-1 line 23 244-3-1 line 23 244-3-1 loss of deposit 09 deposit 09 deposit 1998 (09.09.1998) ATCC 203252 245-4 Additional Indications NONE 104 description on: These indications are Made 105 246-3-1 line 23 247-3-1 line 23 248-3-1 loss of deposit 1998 (09.09.1998) ATCC 203252 248-3-1 loss of deposit 1998 (09.09.1998) ATCC 203252 ATTENDATE OF TWO INTITUT		, , , , , , , , , , , , , , , , , , , ,	
243-2 line 22 243-3 line 223 243-3-1 line 224 243-3-1 line 243-3-2 line depositary institution 243-3-2 line 243-3-3 line depositary institution 243-3-2 line 243-3-3 line 243-3-3 line 243-3-3 line 243-3-4 line 243-3-3 line 243-3-4 line 2			
243-3 Identification of Deposit Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States of America 20110-2209United States 20110-2209United St	243-1	page	103
243-3-1 Name of depositary institution 243-3-2 Address of depositary institution 243-3-3 Date of deposit 243-3-3 Date of deposit 243-3-4 Accession Number 243-5 Designated States for Which indications are indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 244-3-1 Date of deposit 243-3 Date of deposit 244-3-1 Date of deposit and indications are Made 244-3-1 Date of deposit and indications are Made 244-3-1 Date of deposit and indication of Deposit 244-3-1 Date of deposit and indications are Made 244-3-3 Date of deposit and indications are Made 244-3-4 Accession Number 244-3-5 Designated States for Which indications are made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 244-3-1 Name of depositary institution 244-3-2 Date of deposit and indications are made below related to the deposited microorganism(s) or other biological material referred to in the description on: 244-3-3 Date of deposit and indications are Made 244-5 Designated States for Which indications are Made 244-6 Designated States for Which indications are Made 244-7 Designated States for Which indications are Made 244-8 Separate Furnishing of Indications 245-1 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103 104 105 105 107 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 10801 University Blvd. of Manassas, Virginia 20110-2209United States of America 10801 University Blvd. of Manassas, Virginia 20110-2209Un	243-2	line	22
243-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 99 September 1998 (09.09.1998) ATCC 203252 243-4 Accession Number ATCC 203252 243-5 Designated States for Which Indications are Made to the International Bureau later 244 The indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 244-3 Identification of Deposit Name of depositary institution Address of deposit 17 November 1998 (17.11.1998) ATCC 203476 NONE 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 103 104-3-3 Date of deposit 17 November 1998 (17.11.1998) ATCC 203476 NONE 17 November 1998 (17.11.1998) ATCC 203476 NONE 244-4 Additional Indications These indications will be submitted to the International Bureau later 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications will be submitted to the International Bureau later 246 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103		· ·	
Virginia 20110-2209United States of America 243-3-3 Date of deposit 243-3-4 Accession Number 243-6 Separate Furnishing of Indications These indications will be submitted to the Indications made below relate to the deposited microorganism(s) or other biological material referred to In 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 244-3-3 Date of deposit 244-3-4 Accession Number Virginia 20110-2209United States of America 254-5 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 103 234-4-3 Identification of Deposit 244-3-1 Identification of Deposit 244-3-1 Varne of depositary institution 244-3-2 Address of depositary institution 244-3-3 Date of deposit 244-3-4 Accession Number ATCC 203476 NONE 244-4 Additional Indications These indications will be submitted to the Indications are Made 244-5 Designated States for Which Indications are Made 244-5 Designated States for Which Indications are Made These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 246-1 page 247-2 International Bureau later 248-3 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 249-3 The indications made and the properties to the deposited microorganism(s) or other biological material referred to in the description on: 240-3 Date of deposit 241-4 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 246-1 Page The Made States for Which Indications made and the properties of the description on: 247-3 Date of deposit		, ,	American Type Culture Collection
America 09 September 1998 (09.09.1998) ATCC 203252 43-3-4 Accession Number ATCC 203252 43-4 Additional Indications NONE 243-5 Designated States for Which Indications are Made 243-6 Separate Furnishing of Indications These indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 244-1 page 103 244-3 Identification of Deposit American Type Culture Collection: 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 Additional Indications NONE ATCC 203476 NONE American Type Culture Collection: 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 103476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 103476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 203476 NONE ATCC 203476 Additional Indications are Made ATCC 103476 Additional Indications are Made ATCC 203476 Additional Indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 4451 page 103	243-3-2	Address of depositary institution	10801 University Blvd., Manassas,
243-3-3 Date of deposit 243-3-4 Accession Number 243-3-4 Additional Indications 243-5 Designated States for Which Indications are Made 243-6 Separate Furnishing of Indications 243-6 The indications will be submitted to the deposited microorganisms or other biological material referred to in the description on: 244-1 page 244-3-1 Identification of Deposit 244-3-2 Address of depositary institution 244-3-3 Date of deposit 244-3-3 Date of deposit 244-3-4 Additional Indications 244-3-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications 244-6 Separate Furnishing of Indications 245-1 page 246-1 The indications will be submitted to the deposited microorganisms or other biological material referred to in the description or: 246-1 The indications and below relate to the International Bureau later 246-1 The indications and below relate to the Indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 246-1 page 247-1 page 248-2 Designated States for Which Indications are Made 249-3 The indications will be submitted to the International Bureau later 248-3 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 248-1 page 249-1 page 249-2 Page 10-3 Page 10-			Virginia 20110-2209United States of
243-3-4 Accession Number ATCC 203252 243-4 Additional Indications NONE 243-5 Designated States for Which Indications are Made 243-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 244 The Indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 244-1 page 244-2 line 244-3-1 Name of depositary institution 244-3-1 Address of depositary institution 244-3-2 Address of deposit 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-4 Additional Indications These indications will be submitted to the International Bureau later 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103			America
243-4 Additional Indications NONE 243-5 Designated States for Which Indications are Made 243-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 244 The Indications made below relate to the deposited microorganism(s) or other biological material referred to In the description on: page 244-1 page 244-2 line 244-3 Identification of Deposit 244-3-1 Name of depositary institution Address of depositary institution 244-3-1 Date of deposit 244-3-3 Date of deposit 244-3-4 Accession Number 244-3 Accession Number 244-4 Additional Indications NONE NONE ATCC 203476 NONE NONE NONE NONE NONE 1 designated States NONE NONE NONE NONE 1 designated States NONE NONE 1 designated States NONE NONE 1 designated States NONE	243-3-3	Date of deposit	09 September 1998 (09.09.1998)
243-5 Designated States for Which Indications are Made 243-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 244 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103 244-1 page 103 244-2 line 23 244-3 Identification of Deposit 244-3-1 Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 20110-2209United States of America 17 November 1998 (17.11.1998) 244-3-1 Date of deposit 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later to the deposited microorganism(s) or other biological material referred to in the description on: 103	243-3-4	Accession Number	ATCC 203252
Indications are Made 243-6 Separate Furnishing of Indications These indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 244-1 page 244-3-1 line 244-3-2 Address of depositary institution 244-3-2 Date of deposit 244-3-3 Date of deposit 244-3-4 Additional Indications 244-3 Accession Number 244-3 Edes Graves of Separate Furnishing of Indications These indications will be submitted to the depositatory in the description on: 245-6 Designated States for Which indications are Made 246-7 The indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103 247-2 Accession Number 246-3 Separate Furnishing of Indications These indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 105 107 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 NONE 11 designated States NONE	243-4	Additional Indications	NONE
These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103 244-2 line 23 244-3 lidentification of Deposit Name of depositary institution Address of depositary institution 244-3-2 Address of depositary institution 244-3-3 Date of deposit 244-3-4 Accession Number 244-3 Additional Indications 17 November 1998 (17.11.1998) ATCC 203476 Additional Indications NONE 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103 247-2 Additional Indications These indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103 248-2 Additional Indications NONE	243-5		all designated States
the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to In the description on: page 103 244-2 line 23 444-3-1 line 23 444-3-2 Address of depositary institution American Type Culture Collection: 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 244-3-3 Date of deposit 17 November 1998 (17.11.1998) 444-3-4 Accession Number ATCC 203476 444-4 Additional Indications NONE 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103	243-6	Separate Furnishing of Indications	NONE
the deposited microorganism(s) or other biological material referred to In the description on: page 103 244-2 line 23 244-3-1 Identification of Deposit Name of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 20110-2209United States of America 17 November 1998 (17.11.1998) 244-3-3 Date of deposit 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which Indications are Made Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103			
244-1 page line 23 244-2 line 23 244-3 lidentification of Deposit Name of depositary institution Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 244-3-3 Date of deposit 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244	the deposited microorganism(s) or other biological material referred to in	
244-3-1 Identification of Deposit 244-3-1 Name of depositary institution 244-3-2 Address of depositary institution 244-3-2 Date of deposit 244-3-3 Date of deposit 244-3-4 Accession Number 244-4 Additional Indications 244-4 Additional Indications 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 244-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 NONE NONE NONE 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 NONE 245-1 page 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) NONE 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) ATCC 203476 NONE 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) NONE 244-3-4 Additional Indications NONE 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) NONE	244-1	•	103
Identification of Deposit Name of depositary institution American Type Culture Collection: 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) Accession Number ATCC 203476 Accession Number ATCC 203476 Additional Indications NONE Additional States for Which Indications are Made Additional Sureau later These indications will be submitted to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103	244-2	line	23
Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 244-3-3 Date of deposit 17 November 1998 (17.11.1998) ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) NONE NONE	244-3	Identification of Deposit	
244-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) 244-3-4 Accession Number 244-4 Additional Indications Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-3-1	Name of depositary institution	American Type Culture Collection:
Virginia 20110-2209United States of America 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-5 Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-3-2	Address of depositary institution	
America 244-3-3 Date of deposit 17 November 1998 (17.11.1998) 244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which Indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103			l · · · · · · · · · · · · · · · · · · ·
244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103			i — -
244-3-4 Accession Number ATCC 203476 244-4 Additional Indications NONE 244-5 Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-3-3	Date of deposit	17 November 1998 (17.11.1998)
244-4 Additional Indications 244-5 Designated States for Which indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-3-4	Accession Number	
indications are Made 244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-4	Additional Indications	
244-6 Separate Furnishing of Indications These indications will be submitted to the International Bureau later 245 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-5		all designated States
the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: page 103	244-6		NONE
The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103		1	
the deposited microorganism(s) or other biological material referred to in the description on: 245-1 page 103	245		
	245	the deposited microorganism(s) or other biological material referred to in	
245-2 line 24	245-1	page	103

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P3330R1 Original (for SUBMISSION) - printed on 01.12.2000 02:57:35 PM 245-3 **Identification of Deposit** 245-3-1 Name of depositary institution American Type Culture Collection 245-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 245-3-3 Date of deposit 04 August 1998 (04.08.1998) 245-3-4 Accession Number ATCC 203094 245-4 Additional Indications NONE 245-5 **Designated States for Which** all designated States Indications are Made 245-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 246-1 page 103 246-2 25 246-3 **Identification of Deposit** 246-3-1 Name of depositary institution American Type Culture Collection 246-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 246-3-3 Date of deposit 15 September 1998 (15.09.1998) 246-3-4 Accession Number ATCC 203235 246-4 Additional Indications NONE 246-5 **Designated States for Which** all designated States Indications are Made 246-6 Separate Furnishing of Indications NONE These indications will be submitted to the International Bureau later 247 The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on: 247-1 page 103 247-2 26 247-3 **Identification of Deposit** 247-3-1 Name of depositary institution American Type Culture Collection 247-3-2 Address of depositary institution 10801 University Blvd., Manassas, Virginia 20110-2209United States of America 247-3-3 Date of deposit 22 September 1998 (22.09.1998) 247-3-4 Accession Number ATCC 203267 247-4 Additional Indications NONE 247-5 Designated States for Which all designated States Indications are Made 247-6 Separate Furnishing of Indications NONE

These indications will be submitted to the International Bureau later

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248	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
248-1	page	103
248-2	line	27
248-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
248-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	·	Virginia 20110-2209United States of
		America
248-3-3	Date of deposit	22 September 1998 (22.09.1998)
248-3-4	Accession Number	ATCC 203282
248-4	Additional Indications	NONE
248-5	Designated States for Which	all designated States
	Indications are Made	all designated States
248-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
249	the International Bureau later The indications made below relate to	
240	the deposited microorganism(s) or other biological material referred to in the description on:	
249-1	page	103
249-2	line	28
249-3	Identification of Deposit	
249-3-1	Name of depositary institution	American Type Culture Collection
249-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
249-3-3	Date of deposit	09 February 1999 (09.02.1999)
249-3-4	Accession Number	ATCC 203657
249-4	Additional Indications	NONE
249-5	Designated States for Which	all designated States
	Indications are Made	
249-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
250	the International Bureau later The indications made below relate to	
200	the deposited microorganism(s) or other biological material referred to in	
250-1	the description on:	103
250-2	line	29
	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
250.2.2	Date of deposit	
	Accession Number	22 September 1998 (22.09.1998)
		ATCC 203276
250-4	Additional Indications	NONE
250-5	Designated States for Which	all designated States

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250-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	
	the International Bureau later	
251	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
251-1	page	103
251-2	line	30
251-3	Identification of Deposit	30
251-3-1	•	Amonicos Muso Cultura Callactica
	Address of depositary institution	American Type Culture Collection
251-5-2	Address of depositary institution	10801 University Blvd., Manassas,
	ĺ	Virginia 20110-2209United States of
		America
251-3-3	Date of deposit	25 August 1998 (25.08.1998)
251-3-4	Accession Number	ATCC 203160
251-4	Additional Indications	NONE
251-5	Designated States for Which Indications are Made	all designated States
251-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	NONE
	the International Bureau later	
252	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
252-1	page	103
252-2	line	31
252-3	Identification of Deposit	
252-3-1	Name of depositary institution	American Type Culture Collection
252-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	i	Virginia 20110-2209United States of
		America
252-3-3	Date of deposit	
	Accession Number	18 August 1998 (18.08.1998)
252-4	Additional Indications	ATCC 203135
		NONE
252-5	Designated States for Which Indications are Made	all designated States
252-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	1012
253	the International Bureau later The indications made below relate to	
200	the deposited microorganism(s) or	
	other biological material referred to in	
252 4	the description on:	
253-1	page	103
253-2	line	32
253-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
253-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
253-3-3	Date of deposit	03 November 1998 (03.11.1998)
253-3-4	Accession Number	ATCC 203459
		MICC 203439

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253-4	Additional Indications	NONE
253-5	Designated States for Which Indications are Made	all designated States
253-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
254	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
254-1	page	103
254-2	line	33
254-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
254-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of America
254-3-3	Date of deposit	22 September 1998 (22.09.1998)
	Accession Number	ATCC 203270
254-4	Additional Indications	NONE
254-5	Designated States for Which Indications are Made	all designated States
254-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
255	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
255-1	page	103
255-2	line	34
255-3	Identification of Deposit	
	Name of depositary institution	American Type Culture Collection
200-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
255 2 2	Data of dense it	America
	Date of deposit Accession Number	12 January 1999 (12.01.1999)
255-4	Additional Indications	ATCC 203573
255-5	Designated States for Which	NONE
	Indications are Made	all designated States
255-6		NONE
	These indications will be submitted to the International Bureau later	
256	The indications made below relate to	The state of the s
	the deposited microorganism(s) or other biological material referred to in the description on:	
256-1	·	103
256-2	line	35

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259	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
259-1	page	103
259-2	line	38
259-3	Identification of Deposit	
259-3-1	Name of depositary institution	American Type Culture Collection
259-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
259-3-3	Date of deposit	27 October 1998 (27.10.1998)
259-3-4	Accession Number	ATCC 203407
259-4	Additional Indications	NONE
259-5	Designated States for Which Indications are Made	all designated States
259-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
260	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in the description on:	
260-1	page	103
260-2	line	39
260-3	Identification of Deposit	
260-3-1	Name of depositary institution	American Type Culture Collection
260-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
	į į	America
	Date of deposit	22 December 1998 (22.12.1998)
	Accession Number	ATCC 203553
260-4	Additional Indications	NONE
260-5	Designated States for Which Indications are Made	all designated States
260-6	Separate Furnishing of Indications	NONE .
	These indications will be submitted to the International Bureau later	
261	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in the description on:	
261-1	page	103
261-2	line	40
261-3	Identification of Deposit	
261-3-1	 	American Type Culture Collection
261-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	22 December 1998 (22.12.1998)
		ATCC 203549
261-4		NONE
261-5	Designated States for Which Indications are Made	all designated States

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261-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to	11012
	the International Bureau later	
262	The indications made below relate to the deposited microorganism(s) or	
	other biological material referred to in	
262.4	the description on:	
262-1 262-2	page	103
262-2	line	41
	Identification of Deposit Name of depositary institution	L
	Address of depositary institution	American Type Culture Collection
202-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
262.2.2	Date of damasis	America
	Date of deposit	22 December 1998 (22.12.1998)
	Accession Number	ATCC 203550
262-4	Additional Indications	NONE
262-5	Designated States for Which Indications are Made	all designated States
262-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
263	The indications made below relate to	
	the deposited microorganism(s) or other biological material referred to in	
202.4	the description on:	
263-1	page 	103
263-2	line	42
263-3	Identification of Deposit Name of depositary institution	
	Address of depositary institution	American Type Culture Collection
203-3-2	Address of depositary institution	10801 University Blvd., Manassas,
	<u> </u>	Virginia 20110-2209United States of
26222	Date of decays	America
	Date of deposit	08 June 1999 (08.06.1999)
	Accession Number	ATCC PTA-204
263-4		NONE
263-5	Designated States for Which Indications are Made	all designated States
263-6		NONE
	These indications will be submitted to	NONE
264	The indications made below relate to	
	the deposited microorganism(s) or	
	other biological material referred to in the description on:	
264-1	page	103
264-2	line	43
264-3	Identification of Deposit	43
	1	American Type Culture Collection
	l	10801 University Blvd., Manassas,
		_ · · · · · · · · · · · · · · · · · · ·
		Virginia 20110-2209United States of
264-3-3	la	America
		29 October 1998 (29.10.1998)
		ATCC 203391

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264-4	Additional Indications	NONE
264-5	Designated States for Which Indications are Made	all designated States
264-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
265	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
265-1	page	103
265-2	line	44
265-3	Identification of Deposit	
265-3-1	The state of the s	American Type Culture Collection
265-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
005.0.5		America
	Date of deposit	23 March 1999 (23.03.1999)
	Accession Number	ATCC 203863
265-4	Additional Indications	NONE
265-5	Designated States for Which Indications are Made	all designated States
265-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
266	The Indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
266-1	page	103
266-2	line	45
266-3	Identification of Deposit	
266-3-1	· · · · · · · · · · · · · · · · · · ·	American Type Culture Collection
266-3-2	Address of depositary institution	10801 University Blvd., Manassas,
		Virginia 20110-2209United States of
		America
	Date of deposit	09 March 1999 (09.03.1999)
	Accession Number	ATCC 203834
266-4		NONE
266-5	Designated States for Which Indications are Made	all designated States
266-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	
267	The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:	
267-1	page	103
267-2	line	46

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267-3	Identification of Deposit	
267-3-1	Name of depositary institution	American Type Culture Collection
267-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of
		America
267-3-3	Date of deposit	20 July 1999 (20.07.1999)
267-3-4	Accession Number	ATCC PTA-382
267-4	Additional Indications	NONE
267-5	Designated States for Which Indications are Made	all designated States
267-6	Separate Furnishing of Indications	NONE
	These indications will be submitted to the International Bureau later	

FOR RECEIVING OFFICE USE ONLY

0-4	This form was received with the international application:	
	(yes or no)	
0-4-1	Authorized officer	
		<u>L</u> .

FOR INTERNATIONAL BUREAU USE ONLY

	This form was received by the international Bureau on:	
0-5-1	Authorized officer	

WHAT IS CLAIMED IS:

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1. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence that encodes an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEO ID NO:34), Figure 36 (SEO ID NO:36), Figure 38 (SEO ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEO ID NO:42), Figure 44 (SEO ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEO ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID

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NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID

NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) and Figure 550 (SEQ ID NO:550).

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2. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence selected from the group consisting of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:3), Figure 5 (SEQ ID NO:5), Figure 7 (SEQ ID NO:7), Figure 9 (SEQ ID NO:9), Figure 11 (SEQ ID NO:11), Figure 13 (SEQ ID NO:13), Figure 15 (SEQ ID NO:15), Figure 17 (SEQ ID NO:17), Figure 19 (SEQ ID NO:19), Figure 21 (SEQ ID NO:21), Figure 23 (SEQ ID NO:23), Figure 25 (SEQ ID NO:25), Figure 27 (SEQ ID NO:27), Figure 29 (SEQ ID NO:29), Figure 31 (SEQ ID NO:31), Figure 33 (SEQ ID NO:33), Figure 35 (SEQ ID NO:35), Figure 37 (SEQ ID NO:37), Figure 39 (SEQ ID NO:39), Figure 41 (SEQ ID NO:41), Figure 43 (SEQ ID NO:43), Figure 45 (SEQ ID NO:45), Figure 47 (SEQ ID NO:47), Figure 49 (SEQ ID NO:49), Figure 51 (SEQ ID NO:51), Figure 53 (SEQ ID NO:53), Figure 55 (SEQ ID NO:55), Figure 57 (SEQ ID NO:57), Figure 59 (SEQ ID NO:59), Figure 61 (SEQ ID NO:61), Figure 63 (SEQ ID NO:63), Figure 65 (SEQ ID NO:65), Figure 67 (SEQ ID NO:67), Figure 69 (SEQ ID NO:69), Figure 71 (SEQ ID NO:71), Figure 73 (SEQ ID NO:73), Figure 75 (SEQ ID NO:75), Figure 77 (SEQ ID NO:77), Figure 79 (SEQ ID NO:79), Figure 81 (SEQ ID NO:81), Figure 83 (SEQ ID NO:83), Figure 85 (SEQ ID NO:85), Figure 87 (SEQ ID NO:87), Figure 89 (SEQ ID NO:89), Figure 91 (SEQ ID NO:91), Figure 93 (SEQ ID NO:93), Figure 95 (SEQ ID NO:95), Figure 97 (SEQ ID NO:97), Figure 99 (SEQ ID NO:99), Figure 101 (SEQ ID NO:101), Figure 103 (SEQ ID NO:103), Figure 105 (SEQ ID NO:105), Figure 107 (SEQ ID NO:107), Figure 109 (SEQ ID NO:109), Figure 111 (SEQ ID NO:111), Figure 113 (SEQ ID NO:113), Figure 115 (SEQ ID NO:115), Figure 117 (SEQ ID NO:117), Figure 119 (SEQ ID NO:119), Figure 121 (SEQ ID NO:121), Figure 123 (SEQ ID NO:123), Figure 125 (SEQ ID NO:125), Figure 127 (SEQ ID NO:127), Figure 129 (SEQ ID NO:129), Figure 131 (SEQ ID NO:131), Figure 133 (SEQ ID NO:133), Figure 135 (SEQ ID NO:135), Figure 137 (SEQ ID NO:137), Figure 139 (SEQ ID NO:1390), Figure 141 (SEQ ID NO:141), Figure 143 (SEQ ID NO:143), Figure 145 (SEQ ID NO:145), Figure 147 (SEQ ID NO:147), Figure 149 (SEQ ID NO:149), Figure 151 (SEQ ID NO:151), Figure 153 (SEQ ID NO:153), Figure 155 (SEQ ID NO:155), Figure 157 (SEQ ID NO:157), Figure 159 (SEQ ID NO:159), Figure 161 (SEQ ID NO:161), Figure 163 (SEQ ID NO:163), Figure 165 (SEQ ID NO:165), Figure 167 (SEQ ID NO:167), Figure 169 (SEQ ID NO:169), Figure 171 (SEQ ID NO:171), Figure 173 (SEQ ID NO:173), Figure 175 (SEQ ID NO:175), Figure 177 (SEQ ID NO:177), Figure 179 (SEQ ID NO:179), Figure 181 (SEQ ID NO:181), Figure 183 (SEQ ID NO:183), Figure 185 (SEQ ID NO:185), Figure 187 (SEQ ID NO:187), Figure 189 (SEQ ID NO:189), Figure 191 (SEQ ID NO:191), Figure 193 (SEQ ID NO:193), Figure 195 (SEQ ID NO:195), Figure 197 (SEQ ID NO:197), Figure 199 (SEQ ID NO:199), Figure 201 (SEQ ID NO:201), Figure 203 (SEQ ID NO:203), Figure 205 (SEQ ID NO:205), Figure 207 (SEQ ID NO:207), Figure 209 (SEQ ID NO:209), Figure 211 (SEQ ID NO:211), Figure 213 (SEQ ID NO:213), Figure 215 (SEQ ID NO:215), Figure 217 (SEQ ID NO:217), Figure 219 (SEQ ID NO:219), Figure 221 (SEQ ID

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NO:221), Figure 223 (SEQ ID NO:223), Figure 225 (SEQ ID NO:225), Figure 227 (SEQ ID NO:227), Figure 229 (SEQ ID NO:229), Figure 231 (SEQ ID NO:231), Figure 233 (SEQ ID NO:233), Figure 235 (SEQ ID NO:235), Figure 237 (SEQ ID NO:237), Figure 239 (SEQ ID NO:239), Figure 241 (SEQ ID NO:241), Figure 243 (SEQ ID NO:243), Figure 245 (SEQ ID NO:245), Figure 247 (SEQ ID NO:247), Figure 249 (SEQ ID NO:249), Figure 251 (SEQ ID NO:251), Figure 253 (SEQ ID NO:253), Figure 255 (SEQ ID NO:255), Figure 257 (SEQ ID NO:257), Figure 259 (SEQ ID NO:259), Figure 261 (SEQ ID NO:261), Figure 263 (SEQ ID NO:263), Figure 265 (SEQ ID NO:265), Figure 267 (SEQ ID NO:267), Figure 269 (SEQ ID NO:269), Figure 271 (SEQ ID NO:271), Figure 273 (SEQ ID NO:273), Figure 275 (SEQ ID NO:275), Figure 277 (SEQ ID NO:277), Figure 279 (SEQ ID NO:279), Figure 281 (SEQ ID NO:281), Figure 283 (SEQ ID NO:283), Figure 285 (SEQ ID NO:285), Figure 287 (SEQ ID NO:287), Figure 289 (SEQ ID NO:289), Figure 291 (SEQ ID NO:291), Figure 293 (SEQ ID NO:293), Figure 295 (SEQ ID NO:295), Figure 297 (SEQ ID NO:297), Figure 299 (SEQ ID NO:299), Figure 301 (SEQ ID NO:301), Figure 303 (SEQ ID NO:303), Figure 305 (SEQ ID NO:305), Figure 307 (SEQ ID NO:307), Figure 309 (SEQ ID NO:309), Figure 311 (SEQ ID NO:311), Figure 313 (SEQ ID NO:313), Figure 315 (SEQ ID NO:315), Figure 317 (SEQ ID NO:317), Figure 319 (SEQ ID NO:319), Figure 321 (SEQ ID NO:321), Figure 323 (SEQ ID NO:323), Figure 325 (SEQ ID NO:325), Figure 327 (SEQ ID NO:327), Figure 329 (SEQ ID NO:329), Figure 331 (SEQ ID NO:331), Figure 333 (SEQ ID NO:333), Figure 335 (SEQ ID NO:335), Figure 337 (SEQ ID NO:337), Figure 339 (SEQ ID NO:339), Figure 341 (SEQ ID NO:341), Figure 343 (SEQ ID NO:343), Figure 345 (SEQ ID NO:345), Figure 347 (SEQ ID NO:347), Figure 349 (SEQ ID NO:349), Figure 351 (SEQ ID NO:351), Figure 353 (SEQ ID NO:353), Figure 355 (SEQ ID NO:355), Figure 357 (SEQ ID NO:357), Figure 359 (SEQ ID NO:359), Figure 361 (SEQ ID NO:361), Figure 363 (SEQ ID NO:363), Figure 365 (SEQ ID NO:365), Figure 367 (SEQ ID NO:367), Figure 369 (SEQ ID NO:369), Figure 371 (SEQ ID NO:371), Figure 373 (SEQ ID NO:373), Figure 375 (SEQ ID NO:375), Figure 377 (SEQ ID NO:377), Figure 379 (SEQ ID NO:379), Figure 381 (SEQ ID NO:381), Figure 383 (SEQ ID NO:383), Figure 385 (SEQ ID NO:385), Figure 387 (SEQ ID NO:387), Figure 389 (SEQ ID NO:389), Figure 391 (SEQ ID NO:391), Figure 393 (SEQ ID NO:393), Figure 395 (SEQ ID NO:395), Figure 397 (SEQ ID NO:397), Figure 399 (SEQ ID NO:399), Figure 401 (SEQ ID NO:401), Figure 403 (SEQ ID NO:403), Figure 405 (SEQ ID NO:405), Figure 407 (SEQ ID NO:407), Figure 409 (SEQ ID NO:409), Figure 411 (SEQ ID NO:411), Figure 413 (SEQ ID NO:413), Figure 415 (SEQ ID NO:415), Figure 417 (SEQ ID NO:417), Figure 419 (SEQ ID NO:419), Figure 421 (SEQ ID NO:421), Figure 423 (SEQ ID NO:423), Figure 425 (SEQ ID NO:425), Figure 427 (SEQ ID NO:427), Figure 429 (SEQ ID NO:429), Figure 431 (SEQ ID NO:431), Figure 433 (SEQ ID NO:433), Figure 435 (SEQ ID NO:435), Figure 437 (SEQ ID NO:437), Figure 439 (SEQ ID NO:439), Figure 441 (SEQ ID NO:441), Figure 443 (SEQ ID NO:443), Figure 445 (SEQ ID NO:445), Figure 447 (SEQ ID NO:447), Figure 449 (SEQ ID NO:449), Figure 451 (SEQ ID NO:451), Figure 453 (SEQ ID NO:453), Figure 455 (SEQ ID NO:455), Figure 457 (SEQ ID NO:457), Figure 459 (SEQ ID NO:459), Figure 461 (SEQ ID NO:461), Figure 463 (SEQ ID NO:463), Figure 465 (SEQ ID NO:465), Figure 467 (SEQ ID NO:467), Figure 469 (SEQ ID NO:469), Figure 471 (SEQ ID NO:471), Figure 473 (SEQ ID NO:473), Figure 475 (SEQ ID NO:475), Figure 477 (SEQ ID NO:477), Figure 479 (SEQ ID NO:479), Figure 481 (SEQ ID NO:481), Figure 483 (SEQ ID NO:483), Figure 485 (SEQ ID NO:485), Figure 487 (SEQ ID

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NO:487), Figure 489 (SEQ ID NO:489), Figure 491 (SEQ ID NO:491), Figure 493 (SEQ ID NO:493), Figure 495 (SEQ ID NO:495), Figure 497 (SEQ ID NO:497), Figure 499 (SEQ ID NO:499), Figure 501 (SEQ ID NO:501), Figure 503 (SEQ ID NO:503), Figure 505 (SEQ ID NO:505), Figure 507 (SEQ ID NO:507), Figure 509 (SEQ ID NO:509), Figure 511 (SEQ ID NO:511), Figure 513 (SEQ ID NO:513), Figure 515 (SEQ ID NO:515), Figure 517 (SEQ ID NO:517), Figure 519 (SEQ ID NO:519), Figure 521 (SEQ ID NO:521), Figure 523 (SEQ ID NO:523), Figure 525 (SEQ ID NO:525), Figure 527 (SEQ ID NO:527), Figure 529 (SEQ ID NO:529), Figure 531 (SEQ ID NO:531), Figure 533 (SEQ ID NO:533), Figure 535 (SEQ ID NO:535), Figure 537 (SEQ ID NO:537), Figure 539 (SEQ ID NO:539), Figure 541 (SEQ ID NO:541), Figure 543 (SEQ ID NO:543), Figure 545 (SEQ ID NO:545), Figure 547 (SEQ ID NO:547) and Figure 549 (SEQ ID NO:549).

Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence

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selected from the group consisting of the full-length coding sequence of the nucleotide sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:3), Figure 5 (SEQ ID NO:5), Figure 7 (SEQ ID NO:7), Figure 9 (SEQ ID NO:9), Figure 11 (SEQ ID NO:11), Figure 13 (SEQ ID NO:13), Figure 15 (SEQ ID NO:15), Figure 17 (SEQ ID NO:17), Figure 19 (SEQ ID NO:19), Figure 21 (SEQ ID NO:21), Figure 23 (SEQ ID NO:23), Figure 25 (SEQ ID NO:25), Figure 27 (SEQ ID NO:27), Figure 29 (SEQ ID NO:29), Figure 31 (SEQ ID NO:31), Figure 33 (SEQ ID NO:33), Figure 35 (SEQ ID NO:35), Figure 37 (SEQ ID NO:37), Figure 39 (SEQ ID NO:39), Figure 41 (SEQ ID NO:41), Figure 43 (SEQ ID NO:43), Figure 45 (SEQ ID NO:45), Figure 47 (SEQ ID NO:47), Figure 49 (SEQ ID NO:49), Figure 51 (SEQ ID NO:51), Figure 53 (SEQ ID NO:53), Figure 55 (SEQ ID NO:55), Figure 57 (SEQ ID NO:57), Figure 59 (SEQ ID NO:59), Figure 61 (SEQ ID NO:61), Figure 63 (SEQ ID NO:63), Figure 65 (SEQ ID NO:65), Figure 67 (SEQ ID NO:67), Figure 69 (SEQ ID NO:69), Figure 71 (SEQ ID NO:71), Figure 73 (SEQ ID NO:73), Figure 75 (SEQ ID NO:75), Figure 77 (SEQ ID NO:77), Figure 79 (SEQ ID NO:79), Figure 81 (SEQ ID NO:81), Figure 83 (SEQ ID NO:83), Figure 85 (SEQ ID NO:85), Figure 87 (SEQ ID NO:87), Figure 89 (SEQ ID NO:89), Figure 91 (SEQ ID NO:91), Figure 93 (SEQ ID NO:93), Figure 95 (SEQ ID NO:95), Figure 97 (SEQ ID NO:97), Figure 99 (SEQ ID NO:99), Figure 101 (SEQ ID NO:101), Figure 103 (SEQ ID NO:103), Figure 105 (SEQ ID NO:105), Figure 107 (SEQ ID NO:107), Figure 109 (SEQ ID NO:109), Figure 111 (SEQ ID NO:111), Figure 113 (SEQ ID NO:113), Figure 115 (SEQ ID NO:115), Figure 117 (SEQ ID NO:117), Figure 119 (SEQ ID NO:119), Figure 121 (SEQ ID NO:121), Figure 123 (SEQ ID NO:123), Figure 125 (SEQ ID NO:125), Figure 127 (SEQ ID NO:127), Figure 129 (SEQ ID NO:129), Figure 131 (SEQ ID NO:131), Figure 133 (SEQ ID NO:133), Figure 135 (SEQ ID NO:135), Figure 137 (SEQ ID NO:137), Figure 139 (SEQ ID NO:1390), Figure 141 (SEQ ID NO:141), Figure 143 (SEQ ID NO:143), Figure 145 (SEQ ID NO:145), Figure 147 (SEQ ID NO:147), Figure 149 (SEQ ID NO:149), Figure 151 (SEQ ID NO:151), Figure 153 (SEQ ID NO:153), Figure 155 (SEQ ID NO:155), Figure 157 (SEQ ID NO:157), Figure 159 (SEQ ID NO:159), Figure 161 (SEQ ID NO:161), Figure 163 (SEQ 1D NO:163), Figure 165 (SEQ ID NO:165), Figure 167 (SEQ ID NO:167), Figure 169 (SEQ ID NO:169), Figure 171 (SEQ ID NO:171), Figure 173 (SEQ ID NO:173), Figure 175 (SEQ ID NO:175), Figure 177 (SEQ ID NO:177), Figure 179 (SEQ ID NO:179), Figure 181 (SEQ ID NO:181), Figure 183 (SEQ ID NO:183), Figure 185 (SEQ ID NO:185), Figure 187 (SEQ ID NO:187), Figure 189 (SEQ ID NO:189), Figure 191 (SEQ

ID NO:191), Figure 193 (SEQ ID NO:193), Figure 195 (SEQ ID NO:195), Figure 197 (SEQ ID NO:197), Figure 199 (SEQ ID NO:199), Figure 201 (SEQ ID NO:201), Figure 203 (SEQ ID NO:203), Figure 205 (SEQ ID NO:205), Figure 207 (SEQ ID NO:207), Figure 209 (SEQ ID NO:209), Figure 211 (SEQ ID NO:211), Figure 213 (SEQ ID NO:213), Figure 215 (SEQ ID NO:215), Figure 217 (SEQ ID NO:217), Figure 219 (SEQ ID NO:219), Figure 221 (SEQ ID NO:221), Figure 223 (SEQ ID NO:223), Figure 225 (SEQ ID NO:225), Figure 227 (SEQ ID NO:227), Figure 229 (SEQ ID NO:229), Figure 231 (SEQ ID NO:231), Figure 233 (SEQ 5 ID NO:233), Figure 235 (SEQ ID NO:235), Figure 237 (SEQ ID NO:237), Figure 239 (SEQ ID NO:239), Figure 241 (SEQ ID NO:241), Figure 243 (SEQ ID NO:243), Figure 245 (SEQ ID NO:245), Figure 247 (SEQ ID NO:247), Figure 249 (SEQ ID NO:249), Figure 251 (SEQ ID NO:251), Figure 253 (SEQ ID NO:253), Figure 255 (SEQ ID NO:255), Figure 257 (SEQ ID NO:257), Figure 259 (SEQ ID NO:259), Figure 261 (SEQ 10 ID NO:261), Figure 263 (SEQ ID NO:263), Figure 265 (SEQ ID NO:265), Figure 267 (SEQ ID NO:267), Figure 269 (SEQ ID NO:269), Figure 271 (SEQ ID NO:271), Figure 273 (SEQ ID NO:273), Figure 275 (SEQ ID NO:275), Figure 277 (SEQ ID NO:277), Figure 279 (SEQ ID NO:279), Figure 281 (SEQ ID NO:281), Figure 283 (SEQ ID NO:283), Figure 285 (SEQ ID NO:285), Figure 287 (SEQ ID NO:287), Figure 289 (SEQ ID NO:289), Figure 291 (SEQ ID NO:291), Figure 293 (SEQ ID NO:293), Figure 295 (SEQ ID NO:295), 15 Figure 297 (SEQ ID NO:297), Figure 299 (SEQ ID NO:299), Figure 301 (SEQ ID NO:301), Figure 303 (SEQ ID NO:303), Figure 305 (SEQ ID NO:305), Figure 307 (SEQ ID NO:307), Figure 309 (SEQ ID NO:309), Figure 311 (SEQ ID NO:311), Figure 313 (SEQ ID NO:313), Figure 315 (SEQ ID NO:315), Figure 317 (SEQ ID NO:317), Figure 319 (SEQ ID NO:319), Figure 321 (SEQ ID NO:321), Figure 323 (SEQ ID NO:323), Figure 325 (SEQ ID NO:325), Figure 327 (SEQ ID NO:327), Figure 329 (SEQ ID NO:329), Figure 331 (SEQ 20 ID NO:331), Figure 333 (SEQ ID NO:333), Figure 335 (SEQ ID NO:335), Figure 337 (SEQ ID NO:337), Figure 339 (SEQ ID NO:339), Figure 341 (SEQ ID NO:341), Figure 343 (SEQ ID NO:343), Figure 345 (SEQ ID NO:345), Figure 347 (SEQ ID NO:347), Figure 349 (SEQ ID NO:349), Figure 351 (SEQ ID NO:351), Figure 353 (SEQ ID NO:353), Figure 355 (SEQ ID NO:355), Figure 357 (SEQ ID NO:357), Figure 359 (SEQ ID NO:359), Figure 361 (SEQ ID NO:361), Figure 363 (SEQ ID NO:363), Figure 365 (SEQ ID NO:365), Figure 367 (SEQ ID NO:367), Figure 369 (SEQ ID NO:369), Figure 371 (SEQ ID NO:371), Figure 373 (SEQ 25 ID NO:373), Figure 375 (SEQ ID NO:375), Figure 377 (SEQ ID NO:377), Figure 379 (SEQ ID NO:379), Figure 381 (SEQ ID NO:381), Figure 383 (SEQ ID NO:383), Figure 385 (SEQ ID NO:385), Figure 387 (SEQ ID NO:387), Figure 389 (SEQ ID NO:389), Figure 391 (SEQ ID NO:391), Figure 393 (SEQ ID NO:393), Figure 395 (SEQ ID NO:395), Figure 397 (SEQ ID NO:397), Figure 399 (SEQ ID NO:399), Figure 401 (SEQ ID NO:401), Figure 403 (SEQ ID NO:403), Figure 405 (SEQ ID NO:405), Figure 407 (SEQ ID NO:407), 30 Figure 409 (SEQ ID NO:409), Figure 411 (SEQ ID NO:411), Figure 413 (SEQ ID NO:413), Figure 415 (SEQ ID NO:415), Figure 417 (SEQ ID NO:417), Figure 419 (SEQ ID NO:419), Figure 421 (SEQ ID NO:421), Figure 423 (SEQ ID NO:423), Figure 425 (SEQ ID NO:425), Figure 427 (SEQ ID NO:427), Figure 429 (SEQ ID NO:429), Figure 431 (SEQ ID NO:431), Figure 433 (SEQ ID NO:433), Figure 435 (SEQ ID NO:435), Figure 437 (SEQ ID NO:437), Figure 439 (SEQ ID NO:439), Figure 441 (SEQ ID NO:441), Figure 443 (SEQ 35 ID NO:443), Figure 445 (SEQ ID NO:445), Figure 447 (SEQ ID NO:447), Figure 449 (SEQ ID NO:449), Figure 451 (SEQ ID NO:451), Figure 453 (SEQ ID NO:453), Figure 455 (SEQ ID NO:455), Figure 457 (SEQ

ID NO:457), Figure 459 (SEQ ID NO:459), Figure 461 (SEQ ID NO:461), Figure 463 (SEQ ID NO:463), Figure 465 (SEQ ID NO:465), Figure 467 (SEQ ID NO:467), Figure 469 (SEQ ID NO:469), Figure 471 (SEQ ID NO:471), Figure 473 (SEQ ID NO:473), Figure 475 (SEQ ID NO:475), Figure 477 (SEQ ID NO:477), Figure 479 (SEQ ID NO:479), Figure 481 (SEQ ID NO:481), Figure 483 (SEQ ID NO:483), Figure 485 (SEQ ID NO:485), Figure 487 (SEQ ID NO:487), Figure 489 (SEQ ID NO:489), Figure 491 (SEQ ID NO:491), Figure 493 (SEQ ID NO:493), Figure 495 (SEQ ID NO:495), Figure 497 (SEQ ID NO:497), Figure 499 (SEQ ID NO:499), Figure 501 (SEQ ID NO:501), Figure 503 (SEQ ID NO:503), Figure 505 (SEQ ID NO:505), Figure 507 (SEQ ID NO:507), Figure 509 (SEQ ID NO:509), Figure 511 (SEQ ID NO:511), Figure 513 (SEQ ID NO:513), Figure 515 (SEQ ID NO:515), Figure 517 (SEQ ID NO:517), Figure 519 (SEQ ID NO:519), Figure 521 (SEQ ID NO:521), Figure 523 (SEQ ID NO:523), Figure 525 (SEQ ID NO:525), Figure 527 (SEQ ID NO:527), Figure 529 (SEQ ID NO:529), Figure 531 (SEQ ID NO:531), Figure 533 (SEQ ID NO:533), Figure 535 (SEQ ID NO:535), Figure 537 (SEQ ID NO:537), Figure 539 (SEQ ID NO:539), Figure 541 (SEQ ID NO:541), Figure 543 (SEQ ID NO:543), Figure 545 (SEQ ID NO:545), Figure 547 (SEQ ID NO:547) and Figure 549 (SEQ ID NO:549).

- 4. Isolated nucleic acid having at least 80% nucleic acid sequence identity to the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 7.
 - 5. A vector comprising the nucleic acid of Claim 1.

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- 20 6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
 - 7. A host cell comprising the vector of Claim 5.
- 25 8. The host cell of Claim 7, wherein said cell is a CHO cell.
 - 9. The host cell of Claim 7, wherein said cell is an E. coli.
 - 10. The host cell of Claim 7, wherein said cell is a yeast cell.
 - 11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
- 35
 12. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10),

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Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEO ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEO ID NO:28), Figure 30 (SEO ID NO:30), Figure 32 (SEO ID NO:32), Figure 34 (SEO ID NO:34), Figure 36 (SEO ID NO:36), Figure 38 (SEO ID NO:38), Figure 40 (SEO ID NO:40), Figure 42 (SEO ID NO:42), Figure 44 (SEO ID NO:44), Figure 46 (SEO ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEO ID NO:58), Figure 60 (SEO ID NO:60), Figure 62 (SEO ID NO:62), Figure 64 (SEO ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEO ID NO:72), Figure 74 (SEO ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEO ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEO ID NO:116), Figure 118 (SEO ID NO:118), Figure 120 (SEO ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEO ID NO:124), Figure 126 (SEO ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEO ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEO ID NO:144), Figure 146 (SEO ID NO:146), Figure 148 (SEO ID NO:148), Figure 150 (SEO ID NO:150), Figure 152 (SEO ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEO ID NO:158), Figure 160 (SEO ID NO:160), Figure 162 (SEO ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEO ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEO ID NO:208), Figure 210 (SEO ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEO ID NO:256), Figure 258 (SEO ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure

284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID 5 NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 10 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID 15 NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 20 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEO ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) and

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Figure 550 (SEQ ID NO:550).

13. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence encoded by the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 7.

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- 14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.
- 15. The chimeric molecule of Claim 14, wherein said heterologous amino acid sequence is an epitope tag sequence.
 - 16. The chimeric molecule of Claim 14, wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.
- 15 An antibody which specifically binds to a polypeptide according to Claim 12.
 - 18. The antibody of Claim 17, wherein said antibody is a monoclonal antibody, a humanized antibody or a single-chain antibody.

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- 19. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:
- a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (a) (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEO ID NO:90), Figure 92 (SEO ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:128), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ

ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), 5 Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ 10 ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), 15 Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ 20 ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), 25 Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ 30 ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ

ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), lacking its associated signal peptide;

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(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:56), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:96), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:99), Figure 99 (SEQ ID NO:99), Figure 90 (SEQ ID NO:99), Figure 90 (SEQ ID NO:99), Figure 100 (SEQ ID NO:90), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 99 (SEQ ID NO:98), Figure 99 (SEQ ID NO:98), Figure 99 (SEQ ID NO:98), Figure 100 (SEQ ID NO:96),

Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ 5 ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), 10 Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ 15 ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), 20 Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ 25 ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), 30 Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ 35 ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366),

Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ 5 ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), 10 Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ 15 ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEO ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), 20 Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ 25 ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), with its associated signal peptide; or

(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:66), Figure 60 (SEQ ID NO:60), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 78 (SEQ ID NO:76), Figure 79 (SEQ ID

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NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEO ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEO ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEO ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEO ID NO:256), Figure 258 (SEO ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268). Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEO ID NO:312), Figure 314 (SEO ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ

ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEO ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEO ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEO ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEO ID NO:522), Figure 524 (SEO ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEO ID NO:550), lacking its associated signal peptide.

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- 20. An isolated polypeptide having at least 80% amino acid sequence identity to:
- an amino acid sequence of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID

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NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEO ID NO:52), Figure 54 (SEO ID NO:54), Figure 56 (SEO ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:128), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312),

Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ 1D NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), 5 Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), 10 Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ 15 ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), 20 Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ 25 ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), 30 Figure 524 (SEO ID NO:524), Figure 526 (SEO ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550). lacking its associated signal peptide;

(b) an amino acid sequence of an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ

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ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID

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NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEO ID NO:334), Figure 336 (SEO ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEO ID NO:354), Figure 356 (SEO ID NO:356), Figure 358 (SEO ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEO ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEO ID NO:418), Figure 420 (SEO ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEO ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEO ID NO:474), Figure 476 (SEO ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEO ID NO:530), Figure 532 (SEO ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), with its associated signal peptide; or

an amino acid sequence of an extracellular domain of the polypeptide shown in Figure 2 (SEQ (c) ID NO:2), Figure 4 (SEO ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 5 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 10 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID 15 NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 20 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID 25 NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 30 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure

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270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEO ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure

536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), lacking its associated signal peptide.

21. A method of detecting a PRO1801 polypeptide in a sample suspected of containing a PRO1801 polypeptide, said method comprising contacting said sample with a PRO1114 or PRO4978 polypeptide and determining the formation of a PRO1801/PRO1114 or PRO1801/PRO4978 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1801 polypeptide in said sample.

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- 22. The method according to Claim 21, wherein said sample comprises cells suspected of expressing said PRO1801 polypeptide.
 - 23. The method according to Claim 21, wherein said PRO1114 or PRO4978 polypeptide is labeled with a detectable label.
- The method according to Claim 21, wherein said PRO1114 or PRO4978 polypeptide is attached to a solid support.
 - 25. A method of detecting a PRO1114 or PRO4978 polypeptide in a sample suspected of containing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said sample with a PRO1801 polypeptide and determining the formation of a PRO1801/PRO1114 or PRO1801/PRO4978 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 or PRO4978 polypeptide in said sample.
 - 26. The method according to Claim 25, wherein said sample comprises cells suspected of expressing said PRO1114 or PRO4978 polypeptide.
 - 27. The method according to Claim 25, wherein said PRO1801 polypeptide is labeled with a detectable label.
- The method according to Claim 25, wherein said PRO1801 polypeptide is attached to a solid support.
- 29. A method of linking a bioactive molecule to a cell expressing a PRO1801 polypeptide, said method comprising contacting said cell with a PRO1114 or PRO4978 polypeptide that is bound to said bioactive molecule and allowing said PRO1801 and said PRO1114 or PRO4978 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

30. The method according to Claim 29, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

31. The method according to Claim 29, wherein said bioactive molecule causes the death of said cell.

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32. A method of linking a bioactive molecule to a cell expressing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said cell with a PRO1801 polypeptide that is bound to said bioactive molecule and allowing said PRO1801 and said PRO1114 or PRO4978 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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- 33. The method according to Claim 32, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.
- 34. The method according to Claim 32, wherein said bioactive molecule causes the death of said cell.
 - 35. A method of modulating at least one biological activity of a cell expressing a PRO1801 polypeptide, said method comprising contacting said cell with a PRO1114 or PRO4978 polypeptide or an anti-PRO1801 polypeptide antibody, whereby said PRO1114 or PRO4978 polypeptide or anti-PRO1801 polypeptide antibody binds to said PRO1801 polypeptide, thereby modulating at least one biological activity of said cell.
 - 36. The method according to Claim 35, wherein said cell is killed.
- 37. A method of modulating at least one biological activity of a cell expressing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said cell with a PRO1801 polypeptide or an anti-PRO1114 or anti-PRO4978 polypeptide antibody, whereby said PRO1801 polypeptide or anti-PRO1114 or anti-PRO4978 polypeptide antibody binds to said PRO1114 or PRO4978 polypeptide, thereby modulating at least one biological activity of said cell.
- 30 38. The method according to Claim 37, wherein said cell is killed.
 - 39. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO100 polypeptide and determining the formation of a PRO100/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

40. The method according to Claim 39, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

41. The method according to Claim 39, wherein said PRO100 polypeptide is labeled with a detectable label.

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- 42. The method according to Claim 39, wherein said PRO100 polypeptide is attached to a solid support.
- 43. A method of detecting a PRO100 polypeptide in a sample suspected of containing a PRO100 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO100/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO100 polypeptide in said sample.
- 44. The method according to Claim 43, wherein said sample comprises cells suspected of expressing said PRO100 polypeptide.
 - 45. The method according to Claim 43, wherein said PRO1114 polypeptide is labeled with a detectable label.
- 20 46. The method according to Claim 43, wherein said PRO1114 polypeptide is attached to a solid support.
 - 47. A method of linking a bioactive molecule to a cell expressing a PRO100 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO100 and said PRO1114 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.
 - 48. The method according to Claim 47, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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- 49. The method according to Claim 47, wherein said bioactive molecule causes the death of said cell.
- 50. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO100 polypeptide that is bound to said bioactive molecule and allowing said PRO100 and said PRO1114 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

51. The method according to Claim 50, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

52. The method according to Claim 50, wherein said bioactive molecule causes the death of said cell.

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53. A method of modulating at least one biological activity of a cell expressing a PRO100 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO100 polypeptide antibody, whereby said PRO1114 polypeptide or anti-PRO100 polypeptide antibody binds to said PRO100 polypeptide, thereby modulating at least one biological activity of said cell.

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- 54. The method according to Claim 53, wherein said cell is killed.
- 55. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO100 polypeptide or an anti-PRO1114 polypeptide antibody, whereby said PRO100 polypeptide or anti-PRO1114 polypeptide antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.
 - 56. The method according to Claim 55, wherein said cell is killed.
- 57. A method for stimulating the release of TNF-α from human blood, said method comprising contacting said blood with a PRO195, PRO202, PRO215, PRO221, PRO217, PRO222, PRO198, PRO245, PRO172, PRO265, PRO266, PRO344, PRO337, PRO322, PRO1286, PRO1279, PRO1338 or PRO1343 polypeptide, wherein the release of TNF-α from said blood is stimulated.
- 58. A method for modulating the uptake of glucose or FFA by skeletal muscle cells, said method comprising contacting said cells with a PRO182, PRO366, PRO198, PRO172 or PRO719 polypeptide, wherein the uptake of glucose or FFA by said cells is modulated.
- 59. A method for stimulating the proliferation or differentiation of chondrocyte cells, said method comprising contacting said cells with a PRO182, PRO366, PRO198, PRO1868, PRO202, PRO224, PRO172, PRO301 or PRO1312 polypeptide, wherein the proliferation or differentiation of said cells is stimulated.
 - 60. A method for modulating the uptake of glucose or FFA by adipocyte cells, said method comprising contacting said cells with a PRO202, PRO211, PRO344 or PRO1338 polypeptide, wherein the uptake of glucose or FFA by said cells is modulated.

61. A method for stimulating the proliferation of or gene expression in pericyte cells, said method comprising contacting said cells with a PRO366 polypeptide, wherein the proliferation of or gene expression in said cells is stimulated.

- A method for stimulating the release of proteoglycans from cartilage, said method comprising
 contacting said cartilage with a PRO216 polypeptide, wherein the release of proteoglycans from said cartilage is stimulated.
 - 63. A method for stimulating the proliferation of inner ear utricular supporting cells, said method comprising contacting said cells with a PRO172 polypeptide, wherein the proliferation of said cells is stimulated.
 - 64. A method for stimulating the proliferation of T-lymphocyte cells, said method comprising contacting said cells with a PRO344 polypeptide, wherein the proliferation of said cells is stimulated.
- 65. A method for stimulating the release of a cytokine from PBMC cells, said method comprising contacting said cells with a PRO526 or PRO1343 polypeptide, wherein the release of a cytokine from said cells is stimulated.

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- 66. A method for inhibiting the binding of A-peptide to factor VIIA, said method comprising contacting a composition comprising said A-peptide and said factor VIIA with a PRO182 polypeptide, wherein the binding of said A-peptide to said factor VIIA is inhibited.
- 67. A method for inhibiting the differentiation of adipocyte cells, said method comprising contacting said cells with a PRO185 or PRO198 polypeptide, wherein the differentiation of said cells is inhibited.
- A method for stimulating the proliferation of endothelial cells, said method comprising contacting said cells with a PRO222 polypeptide, wherein the proliferation of said cells is inhibited.
 - 69. A method for detecting the presence of tumor in an mammal, said method comprising comparing the level of expression of any PRO polypeptide shown in Table 8 in (a) a test sample of cells taken from said mammal and (b) a control sample of normal cells of the same cell type, wherein a higher level of expression of said PRO polypeptide in the test sample as compared to the control sample is indicative of the presence of tumor in said mammal.
- 70. The method of Claim 69, wherein said tumor is lung tumor, colon tumor, breast tumor,prostate tumor, rectal tumor, cervical tumor or liver tumor.

71. An oligonucleotide probe derived from any of the nucleotide sequences shown in the accompanying figures.

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FIGURE 1

GTTACTCGGTGGTGGCGGAGTCTACGGAAGCCGTTTTCGCTTCACTTTTCCTGGCTGTAGAGC GCTTTCCCCCTGGCGGGTGAGAGTGCAGAGACGAAGGTGCGAG**ATG**AGCACTATGTTCGCGGA CACTCTCCTCATCGTTTTTATCTCTGTGTGCACGGCTCTGCTCGCAGAGGGCATAACCTGGGT CCTGGTTTACAGGACAGACAAGTACAAGAGACTGAAGGCAGAAGTGGAAAAACAGAGTAAAAA ATTGGAAAAGAAGAACAATAACAGAGTCAGCTGGTCGACAACAGAAAAAGAAAATAGA GAGACAAGAAGAAACTGAAGAATAACAACAGAGATCTATCAATGGTTCGAATGAAATCCAT GTTTGCTATTGGCTTTTGTTTTACTGCCCTAATGGGAATGTTCAATTCCATATTTGATGGTAG AGTGGTGGCAAAGCTTCCTTTTACCCCTCTTTCTTACATCCAAGGACTGTCTCATCGAAATCT GCTGGGAGATGACACCACAGACTGTTCCTTCATTTTCCTGTATATTCTCTGTACTATGTCGAT ${\tt TGGATTTCTTGGCCCACCACCTCCTTCTGGGAAGTTCTCT}{\tt TGA}{\tt ACTCAAGAACTCTTTATTTT}$ CTATCATTCTTCTAGACACACACACACACAGGCGCAACTGTTTTGTAGCAAGAGCCATAGG TAGCCTTACTACTTGGGCCTCTTTCTAGTTTTGAATTATTTCTAAGCCTTTTGGGTATGATTA GAGTGAAAATGGCAGCCAGCAAACTTGATAGTGCTTTTGGTCCTAGATGATTTTTTATCAAATA AGTGGATTGATTAGTTAAGTTCAGGTAATGTTTATGTAATGAAAAACAAATAGCATCCTTCTT GTTTCATTACATAAGTATTTTCTGTGGGACCGACTCTCAAGGCACTGTGTATGCCCTGCAAG GTTTGTTTTGTTGTTTTTTTTTTCAAGCCAAATACATGACATAAGATCAATAAAGAGGCCA AATTTTTAGCTGTTTTATGTACAAGGAGAGATCTGTTTCATTTTGTTTTTGCCGTATTTCTAGA AAAA

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FIGURE 2

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 53-57

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FIGURE 3

AGCCGGGGGCGGGTTTGAAGACGCGTCGTTGGGTTTTGGAGGCCGTGAAACAGCCGTTTGAGT $\tt TTGGCTGCGGGTGGAGAACGTTTGTCAGGGGCCCGGCCAAGAAGGAGGCCCGCCTGTTACG \textbf{AT}$ GCTGTCCATGAGTTTCAAGCGGAACCGCAGTGACCGGTTCTACAGCACCCGGTGCTGCGGCTG TTGCCATGTCCGCACCGGGACGATCATCCTGGGGACCTGGTACATGGTAGTAAACCTATTGAT GGCAATTTTGCTGACTGTGGAAGTGACTCATCCAAACTCCATGCCAGCTGTCAACATTCAGTA TGAAGTCATCGGTAATTACTATTCGTCTGAGAGAATGGCTGATAATGCCTGTGTTCTTTTTGC CGTCTCTGTTCTTATGTTTATAATCAGTTCAATGCTGGTTTATGGAGCAATTTCTTATCAAGT GGGTTGGCTGATTCCATTCTTCTGTTACCGACTTTTTGACTTCGTCCTCAGTTGCCTGGTTGC TATTAGTTCTCTCACCTATTTGCCAAGAATCAAAGAATATCTGGATCAACTACCTGATTTTCC CTACAAAGATGACCTCCTGGCCTTGGACTCCAGCTGCCTCCTGTTCATTGTTCTTGTGTTCTT TGCCTTATTCATCATTTTTAAGGCTTATCTAATTAACTGTGTTTTGGAACTGCTATAAATACAT CAACAACCGAAACGTGCCGGAGATTGCTGTGTACCCTGCCTTTGAAAGCACCTCCTCAGTACG CTGCCTGAAGAAATTCTGCCTTTGACAATAAATCCTATACCAGCTTTTTTGTTTATGTTA CAGAATGCTGCAATTCAGGGCTCTTCAAACTTGTTTGATATAAAATATGTTGTCTTTTGTTTA TTAAGTCTTTTACATTTTAATAGTTTTTGAAGACAATCTAGGTTAAGCAAGAGCAAAGTGCCA TTGTTTGCCTTTAATTGGGGGGTGGGAAGGGAAAGAGGGTACTTGCCACATAGTTTCCTTTTT AACTGCACTTTCTTTATATAATCGTTTGCATTTTGTTACTTGCTACCCTGAGTACTTTCAGGA AGACTGACTTAAATATTCGGGGTGAGTAAGTAGTTGGGTATAAGATCTGAACTTTTCATCTGC AGAGGCAAGAAAATATTTGACATTGTGACTTGACTGTGGAAGATGATGGTTGCATGTTTCTA GTTTGTATATGTTTCCATCTTTGTGATAAGATGATTTAATAAATCTCTTTAAATACTAAAAAA AAAAAAAA

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FIGURE 4

MVSMSFKRNRSDRFYSTRCCGCCHVRTGTIILGTWYMVVNLLMAILLTVEVTHPNSMPAVNIQ YEVIGNYYSSERMADNACVLFAVSVLMFIISSMLVYGAISYQVGWLIPFFCYRLFDFVLSCLV AISSLTYLPRIKEYLDQLPDFPYKDDLLALDSSCLLFIVLVFFALFIIFKAYLINCVWNCYKY INNRNVPEIAVYPAFESTSSVRFANL

Important features of the protein:

Transmembrane domain (Possible type II transmembrane protein): amino acids 30-49, 81-100, 111-131, 158-175

N-glycosylation site.

amino acids 9-13

Tyrosine kinase phosphorylation sites.

amino acids 8-16, 193-202

N-myristoylation site.

amino acids 68-74

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FIGURE 5

ACGCACCCGATGCGGGGCTGCGGCCTAGCGGCGCCCCGGCCCCACCGCGCCCCCGGCCCC TGGCCCGACTGCCCCCCGGCCTTCGCTTCGCTCTTTCCCCCGGGACTGCACGCCATCTACGG AGAGTGCCGCCGCCTTTACCCTGACCAGCCGAACCCGCTCCAGGTTACCGCTATCGTCAAGTA CTGGTTGGGTGGCCCAGACCCCTTGGACTATGTTAGCATGTACAGGAATGTGGGGAGCCCTTC TGCTAACATCCCCGAGCACTGGCACTACATCAGCTTCGGCCTGAGTGATCTCTATGGTGACAA CAGAGTCCATGAGTTTACAGGAACAGATGGACCTAGTGGTTTTGGCTTTGAGTTGACCTTTCG TCTGAAGAGAGAAACTGGGGAGTCTGCCCCACCAACATGGCCCGCAGAGTTAATGCAGGGCTT GGCACGATACGTGTTCCAGTCAGAGAACACCTTCTGCAGTGGGGACCATGTGTCCTGGCACAG CCCTTTGGATAACAGTGAGTCAAGAATTCAGCACATGCTGCTGACAGAGGACCCACAGATGCA GCCCGTGCAGACACCCTTTGGGGTAGTTACCTTCCTCCAGATCGTTGGTGTCTCCACTGAAGA GCTACACTCAGCCCAGCAGTGGAACGGGCAGGGCATCCTGGAGCTGCTGCGGACAGTGCCTAT ACACCTGCAAGAGAGAGTTGACAAAGGCATCGAGACAGATGGCTCCAACCTGAGTGGTGTCAG TGCCAAGTGTGCCTGGGATGACCTGAGCCGGCCCCCCGAGGATGACGAGGACAGCCGGAGCAT CTGCATCGGCACACAGCCCCGGCGACTCTCTGGCAAAGACACAGAGCAGATCCGGGAGACCCT GAGGAGAGGACTCGAGATCAACAGCAAACCTGTCCTTCCACCAATCAACCCTCAGCGGCAGAA TGGCCTCGCCCACGACCGGGCCCCGAGCCGCAAAGACAGCCTGGAAAGTGACAGCTCCACGGC CATCATTCCCCATGAGCTGATTCGCACGCGGCAGCTTGAGAGCGTACATCTGAAATTCAACCA GGAGTCCGGAGCCCTCATTCCTCTCTCCCTAAGGGGCAGGCTCCTGCATGGACGCCACTTTAC ATATAAAAGTATCACAGGTGACATGGCCATCACGTTTGTCTCCACGGGAGTGGAAGGCGCCTT TGCCACTGAGGAGCATCCTTACGCGGCTCATGGACCCTGGTTACAACTC**TGA**ACCTATCCTCG GAGCTCTGCCCTCCCGTCCTGGAACGTCTTTCTGCCCTGAGGAGGGTAGTCAGCATCTCCA ATTTTCAGCAGCTCAAGAACCTTGGCCCCCACAGGACTTCGCAGATGTCACATTGCCCCTCAG TCCCCTGAATGCCCTTCGGACCCAACCCCAATTCCCCAAGCCCCTGACCCCCTAGCTGCCGGG GTTCCCACTCCCAGTGCCACAACCCCCTCACCTCCCCTGGCAGCCCTCAGCGAGCCTGAGGC CCAGCACCCGCTGGCTCCCCAGCACATGGTCCCCTCCCATGGGCTGTTGCCCAGGGAACCGGG GCGCGGTGGGAACGAGCTGCTGGCCTCGGCATGTTTCAATAAAGTTGCTGTGCTGGGAG

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FIGURE 6

MAELRPSGAPGPTAPPAPGPTAPPAFASLFPPGLHAIYGECRRLYPDQPNPLQVTAIVKYWLG
GPDPLDYVSMYRNVGSPSANIPEHWHYISFGLSDLYGDNRVHEFTGTDGPSGFGFELTFRLKR
ETGESAPPTWPAELMQGLARYVFQSENTFCSGDHVSWHSPLDNSESRIQHMLLTEDPQMQPVQ
TPFGVVTFLQIVGVCTEELHSAQQWNGQGILELLRTVPIAGGPWLITDMRRGETIFEIDPHLQ
ERVDKGIETDGSNLSGVSAKCAWDDLSRPPEDDEDSRSICIGTQPRRLSGKDTEQIRETLRRG
LEINSKPVLPPINPQRQNGLAHDRAPSRKDSLESDSSTAIIPHELIRTRQLESVHLKFNQESG
ALIPLCLRGRLLHGRHFTYKSITGDMAITFVSTGVEGAFATEEHPYAAHGPWLQL

Important features:

N-glycosylation site.

amino acids 265-268

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FIGURE 7

CGCGAATGAAGTTTGCATTTTCCTCTGTTCTTGAGCCCAGCTTCTTCTCGTCTCCCACCCCAG CTTCCCGGCATTGGAAGAAGGGACCGTCCTCTTCCTTGTCTTGGCCACCCAAATCCTGGTATC GAAAGGGTTGAACGGACCGGAAGTGTGCAGCAGCGACGGGTCCCCAGCTAATCGACGCCGGAA GTAGCAATTACTAGACAAGCATTCCGCCGCCGGCTTCGCT**ATG**GCGGCAATTCCCCCAGATTC CTGGCAGCCACCCAACGTTTACTTGGAGACCAGCATGGGAATCATTGTGCTGGAGCTGTACTG GAAGCATGCTCCAAAGACCTGTAAGAACTTTGCTGAGTTGGCTCGTCGAGGTTACTACAATGG CACAAAATTCCACAGAATTATCAAAGACTTCATGATCCAAGGAGGTGACCCAACAGGGACAGG TCGAGGTGGTGCATCTATCTATGGCAAACAATTTGAAGATGAACTTCATCCAGACTTGAAATT CACGGGGGCTGGAATTCTCGCAATGGCCAATGCGGGGCCAGATACCAATGGCAGCCAGTTCTT TGTGACCCTCGCCCCCACCCAGTGGCTTGACGGCAAACACCCATTTTTGGCCGAGTGTGTCA ${\tt CGACGTGAAGATCATTAAGGCATACCCTTCTGGGGTAGCTTTGCTACCCTCTTGAGCAGCTCTT}$ CTGAGATGGCCCCAGTGAACCAGCTTCTAGATGACATAGAATGACATGTAATGCTAAATTTCA TTTTGGCTTTGCAAGTCATGAAGCTTAGGAGGCCTGGCATCTTGGGTGAGTTAGAGATGGAAG TACATTTTAATAGGATGCTTCTTTTCTCTTCCCCCAGTGCCTAGGTTGCCAGAGCATTTGCAC AAATGCCCCTGTTTATCAATAGGTGACTACTTACTACACATGAACCATAATGCTGCTTCTTGT GCATGTCTGCTCTGATATACGTCGAACAATGTAGCAGCCACTGTCATTTCTCAGTGGTTTTGC ${\tt CTAACCAAACTTCTTCCTAAGGAGATTTATATTCTGGCCTACACAGCAGTCCTTGATGGCTGA}$ CAGCCACAGAATTCCAAACCAAGTAGTGTCTGTCAGCCCTCTTAACTCTGTGCACGCCCTATT AACCAGAACATCAACAGTGCTGTTTCTGACACTTCAGACATCCCACGCAAAGCCACATTGAAT TTTTGCCAAATGAAAAACACATCCAACAATCAAGTTTCTAAGAAGGTGTCAAGTGGGGAATAA TAATAATGTATAATAATCAAGAAATTAGTTTATTAAAAGGAAGCAGAAGCATTGACCATTTTT TCCCAGAGAAGAGGAGAAATCTGTAGTGAGCAAAGGACAGACCATGAATCCTCCTTGAGAAGT AGTACTCTCAGAAAGGAGAAGCGCCACTCAAGTTCTTTTAACCCAAGACTTTAGAGAAATTAG GTCCAAGATTTTTATATGTTCAGTTGTTTATGTATAAAAATAACTTTCTGGATTTTGTGGGGA GGAGCAGGAGGAAGGAAGTTAATACCTATGTAATACATAGAAACTTCCACAATAAAATGCC ATTGATGGTTAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 8

MAAIPPDSWQPPNVYLETSMGIIVLELYWKHAPKTCKNFAELARRGYYNGTKFHRIIKDFMIQ GGDPTGTGRGGASIYGKQFEDELHPDLKFTGAGILAMANAGPDTNGSQFFVTLAPTQWLDGKH TIFGRVCQGIGMVNRVGMVETNSQDRPVDDVKIIKAYPSG

Important features:

N-glycosylation sites:

amino acids 49-52, 108-111

N-myristoylation sites:

amino acids 64-69, 69-74, 143-148

Cyclophilin-type peptidyl-prolyl cis-trans isomerase signature:

amino acids 48-65

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FIGURE 9

CGGACGCGTGGGCGCGCGAGCGCAGCGGTGGGAGGCGGCGACCAGCCGGTTGAGGCCCCAG GCTTGGCCTCACCACA**ATG**TGGCACGAGGCTCGGAAGCATGAGCGGAAGCTTCGAGGCATGAT GGTCGACTACAAGAAGAGGGCGGAGCGGAGACGGGAGTATTATGAAAAGATCAAGAAGGACCC AGCCCAGTTCCTGCAGGTACATGGCCGAGCTTGCAAGGTGCACCTGGATTCTGCAGTCGCCCT GGCCGCTGAGAGCCCTGTTAATATGATGCCCTGGCAGGGGGACACCAACAACATGATTGACCG ATTCGATGTCCGTGCCCACCTGGACCACATCCCCGACTACACCCCCCCTCTGCTCACCACCAT CTCCCCAGAACAGGAGTCGGACGAACGGAAGTGTAACTACGAGCGCTACAGAGGCCTGGTGCA GAACGACTTTGCCGGCATCTCAGAGGAGCAGTGCCTGTACCAGATCTACATTGATGAGTTGTA CGGAGGCCTCCAGAGACCCAGCGAAGATGAGAAGAAGAAGCTGGCAGAGAAGAAGACTTCCAT CGGTTATACCTACGAGGACAGCACGGTGGCCGAGGTAGAGAAGGCGGCAGAAAAGCCAGAGGA GGAGGAGTCAGCGGCCGAGGAGGAGGAGCAACTCGGACGAAGATGAGGTCATCCCCGACATCGA GACTTATGGCATGGCCGACGGTGACTTCGTCAGGATGCTCCGGAAAGACAAGGAGGAGGCAGA GGCCATCAAGCATGCCAAGGCTCTTGAGGAGGAGAAGGCCATGTACTCGGGACGCCGCTCTCG TGCCCGCCGAGACAGCCCCACCTATGACCCCTATAAGCGGTCACCCTCGGAGTCCAGCTCAGA GTCCCGCTCCCGCTCCCCGACCCCGGCCGCGAGGAGAAGATCACGTTCATCACCAG TTTTGGGGGCAGCGATGAGGAGGCAGCCGCAGCCGCTGCTGCCGCAGCAGCATCAGGAGTCAC CACAGGGAAGCCCCCGCACCTCCCCAGCCTGGCGGCCCCGGCCCCGGGACGTAATGCCAGCGC CAGCTCTCGCTCCAGCTCCCGCTCTCGCCGTGGTGGGGGGCTACTACCGTTCCGGCCGCCACGC CCGCTCCCGGTCCCGCTCCTGGTCCCGCTCCCGCTCCCGGCGCTATTCCCGGTCCCG TAGCCGTGGCCGCCGCACTCAGGTGGGGGCTCCCGAGACGGACACCGGTACTCCCGCTCGCC CGCCCGGCGTGGTGGTTACGGGCCCCGGCGCAGAAGCAGGAGCCGCTCCCACTCAGGGGACCG CTACAGGCGGGCGGCCGGGGCCTCAGGCACCACAGCAGTAGCCGCAGCCGCAGCAGCTGGTC CCTCAGCCGTCCCGCAGTCGCAGCCTGACTCGCAGCCGCAGCCCATAGCCCCAGCCCAGCCA GAGCCGCAGCCGCAGCCGCAGCCAGAGCCCCTCGCCATCACCCGCAAGAGAGAAGCT GACCAGGCCGGCCGCGTCCCCTGCTGTGGGCGAGAAGCTGAAAAAGACCGAACCTGCCGCTGG TAAAGAGACAGGAGCTGCCAAAGTCACCCAAGCTGACGCCTCAGGAGAAGCTGAAACTGAGGA TGCAGAAGGCGCTGAACAGGCAGTTCAAGGCGGA<u>TAA</u>GAAGGCGGCACAAGAAAAGATGATCC AGCAGGAGCATGAGCGGCAGGAGCGGGAAGACGAGCTTCGAGCCATGGCCCGCAAGATCCGCA GCCGCTCACCCTCCCCCGATACAGTCGAGAATACAGCTCTTCTCGAAGGCGCTCAAGGTCCC GATCCCGAAGCCCCCATTACCGACATTAGGCAGAAGAGTGGGGGGTGGGGAGGACAAGGGGGT GGGTAAGGGGCTCAAGCTGTGATGCTGCTGGTTTTATCTCTAGTGAAATAAAGTCAAAAGTTA AAAAAAA

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FIGURE 10

MWHEARKHERKLRGMMVDYKKRAERRREYYEKIKKDPAQFLQVHGRACKVHLDSAVALAAESP
VNMMPWQGDTNNMIDRFDVRAHLDHIPDYTPPLLTTISPEQESDERKCNYERYRGLVQNDFAG
ISEEQCLYQIYIDELYGGLQRPSEDEKKKLAEKKASIGYTYEDSTVAEVEKAAEKPEEEESAA
EEESNSDEDEVIPDIDVEVDVDELNQEQVADLNKQATTYGMADGDFVRMLRKDKEEAEAIKHA
KALEEEKAMYSGRRSRRQRREFREKRLRGRKISPPSYARRDSPTYDPYKRSPSESSSESRSS
RSPTPGREEKITFITSFGGSDEEAAAAAAAAAASGVTTGKPPAPPQPGGPAPGRNASARRRSS
SSSSSSSASRTSSSRSSSRSSRSRRGGGYYRSGRHARSRSRSWSRSRSRSRRYSRSRGRR
HSGGGSRDGHRYSRSPARRGGYGPRRRSRSRSHSGDRYRRGGRGLRHHSSSRSSWSLSPSR
SRSLTRSRSHSPSPSQSRSRSRSRSQSPSPSPAREKLTRPAASPAVGEKLKKTEPAAGKETGA
AKVTQADASGEAETEDAEGAEQAVQGG

Important features:

N-glycosylation site:

amino acids 370-373

Glycosaminoglycan attachment site:

amino acids 443-446

cAMP- and cGMP-dependent protein kinase phosphorylation site: amino acids 159-162, 282-285, 291-294, 374-377, 375-378, 430-433,

440-443, 466-469

Casein kinase II phosphorylation site:

amino acids 149-152, 166-169, 171-174, 187-190, 193-196, 195-198, 303-306, 307-310, 335-338, 571-574

N-myristoylation sites:

amino acids 118-123, 229-234, 350-355, 446-451, 586-591

Amidation sites:

amino acids 263-266, 280-283, 438-441

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FIGURE 11

GGTAGGCGCCCCAGACCTGAGACGGGTTGGGACTGGGCTGCGTCACGCGCGGGCTCTAAGCG AAGGCCGCCTGGAAACTTAAATCCCGAGGCGGGCGAACCTGCACCAGACCGCGGACGTCTGTA ATCTCAGAGGCTTGTTTGCTGAGGGTGCCTGCGCAGCTGCGACGGCTGCTGGTTTTGAAAC**AT** GAATCTTTCGCTCGTCCTGGCTGCCTTTTGCTTGGGAATAGCCTCCGCTGTTCCAAAATTTGA CCAAAATTTGGATACAAAGTGGTACCAGTGGAAGGCAACACACAGAAGATTATATGGCGCGAA TGAAGAAGGATGGAGGAGACCAGTGTGGGAAAAGAATATGAAAATGATTGAACTGCACAATGG GGAATACAGCCAAGGGAAACATGGCTTCACAATGGCCATGAATGCTTTTGGTGACATGACCAA TGAAGAATTCAGGCAGATGATGGGTTGCTTTCGAAACCAGAAATTCAGGAAGGGGAAAGTGTT GCCAGTGAAGAATCAGAAACAGTGTGGTTCTTGTTGGGCTTTTTAGTGCGACTGGTGCTCTTGA TTCGCGTCCTCAAGGCAATCAGGGCTGCAATGGTGGCTTCATGGCTAGGGCCTTCCAGTATGT CAAGGAGAACGGAGGCCTGGACTCTGAGGAATCCTATCCATATGTAGCAGTGGATGAAATCTG TAAGTACAGACCTGAGAATTCTGTTGCTAATGACACTGGCTTCACAGTGGTCGCACCTGGAAA GGAGAAGGCCCTGATGAAAGCAGTCGCAACTGTGGGGCCCATCTCCGTTGCTATGGATGCAGG CCATTCGTCCTTCCAGTTCTACAAATCAGGCATTTATTTTGAACCAGACTGCAGCAGCAAAAA CCTGGATCATGGTGTTCTGGTGGTTGGCTACGGCTTTGAAGGAGCAAATTCGAATAACAGCAA GTATTGGCTCGTCAAAAACAGCTGGGGTCCAGAATGGGGCTCGAATGGCTATGTAAAAATAGC TGGATGGTGAGGAGGAGGACTTAAGGACAGCATGTCTGGGGAAATTTTATCTTGAAACTGAC CAAACGCTTATTGTGTAAGATAAACCAGTTGAATCATGGAGGATCCAAGTTGAGATTTTAATT CTGTGACATTTTTACAAGGGTAAAATGTTACCACTACTTTAATTATTGTTATACACAGCTTTA TGATATCAAAGACTCATTGCTTAATTCTAAGACTTTTGAATTTTCATTTTTTAAAAAAGATGTA CAAAACAGTTTGAAATAAATTTTAATTCGTATATA

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FIGURE 12

MNLSLVLAAFCLGIASAVPKFDQNLDTKWYQWKATHRRLYGANEEGWRRAVWEKNMKMIELHN
GEYSQGKHGFTMAMNAFGDMTNEEFRQMMGCFRNQKFRKGKVFREPLFLDLPKSVDWRKKGYV
TPVKNQKQCGSCWAFSATGALEGQMFRKTGKLVSLSEQNLVDCSRPQGNQGCNGGFMARAFQY
VKENGGLDSEESYPYVAVDEICKYRPENSVANDTGFTVVAPGKEKALMKAVATVGPISVAMDA
GHSSFQFYKSGIYFEPDCSSKNLDHGVLVVGYGFEGANSNNSKYWLVKNSWGPEWGSNGYVKI
AKDKNNHCGIATAASYPNV

Important features:

Signal sequence

amino acids 1-17

N-glycosylation sites.

amino acids 2-6, 221-225, 292-296

N-myristoylation sites.

amino acids 13-19, 93-99, 136-142, 145-151, 174-180, 177-183, 180-186, 194-200, 288-294, 324-330

Eukaryotic thiol (cysteine) proteases cysteine active site. amino acids 132-144

Eukaryotic thiol (cysteine) proteases histidine active site. amino acids 275-286

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FIGURE 13

GGCGGCGTCATGTGATCCGCTTCCCTGCTCCTTTAAGCGTCCACAGGCGGCGGAGCGGCCACA ATCACAGCTCCGGGCATTGGGGGAACCCGAGCCGGCTGCGCCGGGGGAATCCGTGCGGGCGCCC TTCCGTCCCGGTCCCATCCTCGCCGCGCTCCAGCACCTCTGAAGTTTTGCAGCGCCCCAGAAAG GAGGCGAGGAAGGAGGGGTGTGTGAGAGGAGGAGCAAAAAGCTCACCCTAAAACATTTATT TCAAGGAGAAAAGGAGAGGGGGGGGCGCAAAA**ATG**GCTGGGGCAATTATAGAAAACATGAGCA CCAAGAAGCTGTGCATTGTTGGTGGGATTCTGCTCGTGTTCCAAATCATCGCCTTTCTGGTGG GAGGCTTGATTGCTCCAGGGCCCACAACGGCAGTGTCCTACATGTCGGTGAAATGTGTGGATG CCCGTAAGAACCATCACAAGACAAAATGGTTCGTGCCTTGGGGACCCAATCATTGTGACAAGA TCCGAGACATTGAAGAGGCAATTCCAAGGGAAATTGAAGCCAATGACATCGTGTTTTCTGTTC ACATTCCCCTCCCCCACATGGAGATGAGTCCTTGGTTCCAATTCATGCTGTTTATCCTGCAGC TGGACATTGCCTTCAAGCTAAACAACCAAATCAGAGAAAATGCAGAAGTCTCCATGGACGTTT CCCTGGCTTACCGTGATGACGCATTTGCTGAGTGGACTGAAATGGCCCATGAAAGAGTACCAC GGAAACTCAAATGCACCTTCACATCTCCCAAGACTCCAGAGCATGAGGGCCGTTACTATGAAT GTGATGTCCTTCCTTTCATGGAAATTGGGTCTGTGGCCCATAAGTTTTACCTTTTAAACATCC GGCTGCCTGTGAATGAGAAGAAGAAAATCAATGTGGGAATTGGGGAGATAAAGGATATCCGGT CGCCCAGCATCTTCATCATTATGGTGTGTATTGGAGGAGGATCACCATGATGTCCCGACCCC CAGTGCTTCTGGAAAAAGTCATCTTTGCCCTTGGGATTTCCATGACCTTTATCAATATCCCAG TGGAATGGTTTTCCATCGGGTTTGACTGGACCTGGATGCTGCTGTTTGGTGACATCCGACAGG GCATCTTCTATGCGATGCTTCTGTCCTTCTGGATCATCTTCTGTGGCGAGCACATGATGGATC AGCACGAGCGGAACCACATCGCAGGGTATTGGAAGCAAGTCGGACCCATTGCCGTTGGCTCCT TCTGCCTCTTCATATTTGACATGTGTGAGAGAGGGGTACAACTCACGAATCCCTTCTACAGTA TCTGGACTACAGACATTGGAACAGAGCTGGCCATGGCCTTCATCATCGTGGCTGGAATCTGCC TCTGCCTCTACTTCCTGTTTCTATGCTTCATGGTATTTCAGGTGTTTCGGAACATCAGTGGGA AGCAGTCCAGCCTGCCAGCTATGAGCAAAGTCCGGCGGCTACACTATGAGGGGCTAATTTTTA GGTTCAAGTTCCTCATGCTTATCACCTTGGCCTGCGCTGCCATGACTGTCATCTTCTTCATCG TTAGTCAGGTAACGGAAGGCCATTGGAAATGGGGCGGCGTCACAGTCCAAGTGAACAGTGCCT TTTTCACAGGCATCTATGGGATGTGGAATCTGTATGTCTTTGCTCTGATGTTCTTGTATGCAC CATCCCATAAAAACTATGGAGAAGACCAGTCCAATGGCGATCTGGGTGTCCATAGTGGGGAAG AACTCCAGCTCACCACCACTATCACCCATGTGGACGGACCCACTGAGATCTACAAGTTGACCC GCAAGGAGGCCCAGGAGTAGGAGGCTGCAGCGCCCGGCTGGGACGGTCTCTCCATACCCCAGC TCTTAGCTGTGGTTTCTTGGACCAGCGGCATGGACATTTGTCAGTTTGCCTTCTGACGGTAGC TTTTGGAGGAAGATTCCTGCAGCCACTAATGCATTGTGTATGATAACAAAAACTCTGGTATGA CACATTTTCTGTGATCATTGTTAATTAGTGACATAGTAACATCTGTAGCAGCTGGTTAGTAAA CCTCATGTGGGGGTGGGGGTGTATTCCTTGGGGGATGGTTTGGGCCGAATGGGGAGTG GAATATTTGACATTTTTCCTGTTTTAAATTCTAGGATAGATTTTAACATCCTTTGCGGTCCCA GTCCAAGGTAGGCTGGTGTCATAGTCTTCTCACTCCTAATCCATGACCACTGTTTTTTTCCTA TTTATATCACCAGGTAGCCTACTGAGTTAATATTTAAGTTGTCAATAGATAAGTGTCCCTGTT TTGTGGCATAATATAACTGAATTTCATGAGAAGATTTATTCCACCAGGGGTATTTCAGCTTTG AAACCAAATCTGTGTATCTAATACTAACCAATCTGTTGGATGTGGATTTTAAAAAAATGTTTGC TAAACTACCCAAGTAAGATTTACTGTATTAAATGGCCTTCGGGTCTGAAAAGCTTTTTTAACC TCTTGCTTAAAATGCGTTTTATTTTGATAAGATACTTCAAATAGCCTCCAAAAGTGTAGATCC

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FIGURE 14

MAGAIIENMSTKKLCIVGGILLVFQIIAFLVGGLIAPGPTTAVSYMSVKCVDARKNHHKTKWF
VPWGPNHCDKIRDIEEAIPREIEANDIVFSVHIPLPHMEMSPWFQFMLFILQLDIAFKLNNQI
RENAEVSMDVSLAYRDDAFAEWTEMAHERVPRKLKCTFTSPKTPEHEGRYYECDVLPFMEIGS
VAHKFYLLNIRLPVNEKKKINVGIGEIKDIRLVGIHQNGGFTKVWFAMKTFLTPSIFIIMVWY
WRRITMMSRPPVLLEKVIFALGISMTFINIPVEWFSIGFDWTWMLLFGDIRQGIFYAMLLSFW
IIFCGEHMMDQHERNHIAGYWKQVGPIAVGSFCLFIFDMCERGVQLTNPFYSIWTTDIGTELA
MAFIIVAGICLCLYFLFLCFMVFQVFRNISGKQSSLPAMSKVRRLHYEGLIFRFKFLMLITLA
CAAMTVIFFIVSQVTEGHWKWGGVTVQVNSAFFTGIYGMWNLYVFALMFLYAPSHKNYGEDQS
NGDLGVHSGEELQLTTTITHVDGPTEIYKLTRKEAQE

Important features of the protein:

Signal peptide:

amino acids 1-42

Transmembrane domains:

amino acids 239-253, 269-284, 302-318, 338-352, 377-399, 434-452, 471-488

N-glycosylation sites.

amino acids 8-12, 406-410

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 254-258

N-myristoylation sites.

amino acids 223-229, 274-280, 305-311, 358-364, 374-380, 386-392, 509-515

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FIGURE 15

GTGAGGGGAACAGCTGATCCGTCTGTTGGGAGGACAGATATCTCAAGGCCAGGATGGAAGAAT CACCACTAAGCCGGGCACCATCCCGTGGTGGAGTCAACTTTCTCAATGTAGCCCGGACCTACA TCCCCAACACCAAGGTGGAATGTCACTACACCCTTCCCCCAGGCACCATGCCCAGTGCCAGTG ACTGGATTGGCATCTTCAAGGTGGAGGCTGCCTGTGTTCGGGATTACCACACATTTGTGTGGT CTTCCGTGCCTGAAAGTACAACTGATGGTTCCCCCATTCACACCAGTGTCCAGTTCCAAGCCA GCTACCTGCCCAAACCAGGAGCTCAGCTCTACCAGTTCCGATATGTGAACCGCCAGGGCCAGG TGTGTGGGCAGAGCCCCCTTTCCAGTTCCGAGAGCCAAGGCCCATGGATGAACTGGTGACCC TGGAGGAGGCTGATGGGGGCTCTGACATCCTGCTGGTTGTCCCCAAGGCAACTGTGTTACAGA ACCAGCTCGATGAGAGCCAGCAAGAACGGAATGACCTGATGCAGCTGAAGCTACAGCTGGAGG GACAGGTGACAGAGCTGAGGAGCCGAGTGCAGGAGCTCGAGAGGGCTCTGGCAACTGCCAGGC AGGAGCACACGGAGCTGATGGAACAGTACAAGGGGATTTTCCCGGTCCCATGGGGAGATCACAG AAGAGAGGGACATCCTGAGCCGGCAACAGGGAGACCATGTGGCACGCATCCTGGAGCTAGAGG ACACAGTGAAGGCCCTGACTCGGGAACAAGAGAAGCTCCTTGGGCAACTGAAAGAAGTACAAG CAGACAAGGAGCAAAGTGAGGCTGAGCTCCAAGTGGCACAACAGGAGAACCATCACTTAAATT TGGACCTGAAGGAGGCGAAGAGCTGGCAAGAGGAGCAGAGTGCTCAGGCTCAGCGACTGAAAG ACAAGGTGGCCCAGATGAAGGACACCCTAGGCCCAGCCGCCGGGGTGGCCGAGCTGGAGC CCTTGAAGGAGCAGCTTCGAGGGGCCCAGGAGCTTGCAGCCTCAAGCCAGCAGAAAGCCACCC TTCTTGGGGAGGAGTTGGCCAGTGCAGCAGCCAGGGACCGCACCATAGCCGAACTACACC AAGAAAATGCCAATGGAGCAAGGAGCGGGCAGGGCTGCTGCAGAGTGTGGAGGCAGAGAAGG ACAAGATCCTGAAGCTGAGTGCAGAGATACTTCGATTGGAGAAGGCAGTTCAGGAGGAGAGGA ${\tt CCCAAAACCAAGTGTTCAAGACTGAGCTGGCCCGGGAGAAGGATTCTAGCCTGGTACAGTTGT}$ CAGAAAGTAAGCGGGAGCTGACAGAGCTGCGGTCAGCCCTGCGTGTGCTCCAGAAGGAAAAGG AGCAGTTACAGGAGGAGAAACAGGAATTGCTAGAGTACATGAGAAAGCTAGAGGCCCGCCTGG AGAAGGTGGCAGATGAGAAGTGGAATGAGGATGCCACCACAGAGGATGAGGAGGCCGCTGTGG GGCTGAGCTGCCCGGCAGCTCTGACAGACTCAGAGGACGAGTCCCCAGAAGACATGAGGCTCC CACCCTATGGCCTTTGTGAGCGTGGAGACCCAGGCTCCTCTCCTGCTGGGCCTCGAGAGGCTT CTCCCCTTGTTGTCATCAGCCAGCCGGCTCCCATTTCTCCTCACCTCTCTGGGCCAGCTGAGG GGGGTGAGGAGCCAACTTACTGCTTCCTGAACTGGGCAGTGCCTTCTATGACATGGCCAGTG GCTTTACAGTGGGTACCCTGTCAGAAACCAGCACTGGGGGCCCTGCCACCCCCACATGGAAGG AGTGTCCTATCTGTAAGGAGCGCTTTCCTGCTGAGAGTGACAAGGATGCCCTGGAGGACCACA TGGATGGACACTTCTTTTCAGCACCCAGGACCCCTTCACCTTTGAG<u>TGA</u>TCTTACTCCCTCG TGCCCATTTTCTATCACACTGGGCTCCATGATATTCTGTTCCCTAAGAACTGCTTCTGTGTGC CCTGTTTTCATCCCAAGATTTCTCACCTTCATCCTCCTACCTGGCTCTTTTGTCCCAGGGAG GGGTCCTGTTCGGAAGCAGTGGCTGAATTTATCCCCTGAAAGTGGTTTTGGAGGAACCGGGAT GGAGGAGGCCTTCCCCTGTGGGAATAGAATCGTCCACTCCTAGCCCTGGTTGCTTCTGATACA CAGCCACTGCACACACACTCACACTCACACTCCCTTGTCTGATGCCCCAAAGCCAATTCCT GGGGCACCCTACCCTCTCTTATTTGGAGTTTCCGTTGGTTTACCTGAGTTTTCTCTGGGGTCT GCACAGAGGCAGCATGGACATCATGGCCTCTCAGGTCCCTTTTGGTTCTCAGTTTCATTG GTTCCTCTTTCTGTTCCCCCATTGACTTCTGTGCCCCACCCTAGCCTTTTCCATAACCTTAGG TATTCAGTTTGGAGGGGTTTTTTTGTATTTTTGAGGATTCCTGTATTCTGTATCCTCTCCTCGC ATCTCCTCACATGGAAAGAAATAATGTATTTGTGCCTTCTGTGAGGAATGGGGGGAACAAGTG GTCCCAGGTATCCCCATTTCCAAGGCCCCCCTCCCTCTCCAGGTCCCCCACAGCAATAAAAG CTTCCCCCTGATATCCATCCCTTTGTAGTTTGAACAAATATATTTATATGATATGTAA

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FIGURE 16

MEESPLSRAPSRGGVNFLNVARTYIPNTKVECHYTLPPGTMPSASDWIGIFKVEAACVRDYHT
FVWSSVPESTTDGSPIHTSVQFQASYLPKPGAQLYQFRYVNRQGQVCGQSPPFQFREPRPMDE
LVTLEEADGGSDILLVVPKATVLQNQLDESQQERNDLMQLKLQLEGQVTELRSRVQELERALA
TARQEHTELMEQYKGISRSHGEITEERDILSRQQGDHVARILELEDDIQTISEKVLTKEVELD
RLRDTVKALTREQEKLLGQLKEVQADKEQSEAELQVAQQENHHLNLDLKEAKSWQEEQSAQAQ
RLKDKVAQMKDTLGQAQQRVAELEPLKEQLRGAQELAASSQQKATLLGEELASAAAARDRTIA
ELHRSRLEVAEVNGRLAELGLHLKEEKCQWSKERAGLLQSVEAEKDKILKLSAEILRLEKAVQ
EERTQNQVFKTELAREKDSSLVQLSESKRELTELRSALRVLQKEKEQLQEEKQELLEYMRKLE
ARLEKVADEKWNEDATTEDEEAAVGLSCPAALTDSEDESPEDMRLPPYGLCERGDPGSSPAGP
REASPLVVISQPAPISPHLSGPAEDSSSDSEAEDEKSVLMAAVQSGGEEANLLLPELGSAFYD
MASGFTVGTLSETSTGGPATPTWKECPICKERFPAESDKDALEDHMDGHFFFSTQDPFTFE

Important features:

Casein kinase II phosphorylation sites:

amino acids 28-31, 43-46, 68-71, 72-75, 129-132, 156-159, 208-211, 239-242, 282-285, 305-308, 376-379, 383-383, 468-471, 520-523, 521-524, 537-540, 539-542, 543-546, 593-596, 595-598, 597-600, 612-615, 639-642, 652-655, 667-670, 683-686

N-myristoylation sites:

amino acids 39-44, 107-112, 204-209, 414-419, 561-566, 613-618

Cell attachment sequence:

amino acids 557-559

Leucine zipper pattern sequence:

amino acids 163-184, 475-496, 482-503

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FIGURE 17

GCAAGTTGGGAATTTTAGACTGTCACTGCACATGGACCTCTGGGAAGACGTCTGGCGAGAGCT AGGCCCACTGGCCCTACAGACGGATCTTGCTGGCTCACCTGTCCCTGTGGAGGTTCCCCTGGG AAGGCAAGATGCCCAACAACAGCACTGCTCTGTCATTGGCCAATGTTACCTACATCACCATGG AAATTTTCATTGGACTCTGCGCCATAGTGGGCAACGTGCTGGTCATCTGCGTGGTCAAGCTGA ACCCCAGCCTGCAGACCACCACCTTCTATTTCATTGTCTCTCTAGCCCTGGCTGACATTGCTG TTGGGGTGCTGGTCATGCCTTTGGCCATTGTTGTCAGCCTGGGCATCACAATCCACTTCTACA GCTGCCTTTTTATGACTTGCCTACTGCTTATCTTTACCCACGCCTCCATCATGTCCTTGCTGG CCATCGCTGTGGACCGATACTTGCGGGTCAAGCTTACCGTCAGATTCAGAATTCCTGGGCTCC TACTCTCCTTGGCTCTCATTTCAGATGCCATGGTCATGGATGAAAAGGTCAAGAAGCTTTG TGCTGGACACGGCTTCTGCCATCTGCAACTACAATGCCCACTACAAGAATCACCCCAAATACT GGTGCCGAGGCTATTTCCGTGACTACTGCAACATCATCGCCTTCTCCCCTAACAGCACCAATC ACACGGGCTGGTACTGGTGTGGCATCCAGCGGGACTTTGCCAGGGATGACATGGATTTTACAG AGCTGATTGTAACTGACGACAAAGGAACCCTGGCCAATGACTTTTGGTCTGGGAAAGACCTAT CAGGCAACAAACCAGAAGCTGCAAGGCTCCCAAAGTTGTCCGCAAGGCTGACCGCTCCAGGA CGTCCATTCTCATCATTTGCATACTGATCACGGGTTTGGGAATCATCTCTGTAATCAGTCATT TGACCAAAAGGAGGAGAAGTCAAAGGAATAGAAGGGTAGGCAACACTTTGAAGCCCTTCTCGC GTGTCCTGACTCCAAAGGAAATGGCTCCTACTGAACAGATG**TGA**CTGAAGATTTTTTTAATTT AGTTCATAAAGTGATGCTACAACAGAATAATCACCATGACAACTGGCCCACACCTCAGAGACT GATTCTGATCTCCCAGGAATTCTGAAGGACCCTCTATCCTTGACAACAATCATTTGCAGCCAG CTGGATTGGGGACCAGGAAATCACTTGTATTTTTGTTAGCCAATAAATTCCTAGCCAGTGTTGA ATGAAAAAAAAAAAAA

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FIGURE 18

MPNNSTALSLANVTYITMEIFIGLCAIVGNVLVICVVKLNPSLQTTTFYFIVSLALADIAVGV LVMPLAIVVSLGITIHFYSCLFMTCLLLIFTHASIMSLLAIAVDRYLRVKLTVRFRIPGLPGC ILSFQLKVCFLPVMWLFILLSLALISDAMVMDEKVKRSFVLDTASAICNYNAHYKNHPKYWCR GYFRDYCNIIAFSPNSTNHVALRDTGNQLIVTMSCLTKEDTGWYWCGIQRDFARDDMDFTELI VTDDKGTLANDFWSGKDLSGNKTRSCKAPKVVRKADRSRTSILIICILITGLGIISVISHLTK RRRSQRNRRVGNTLKPFSRVLTPKEMAPTEQM

Important features of the protein:

Transmembrane domains:

amino acids 16-35, 62-80, 89-101, 134-152, 292-311

N-glycosylation sites.

amino acids 3-7, 4-8, 12-16, 204-208, 273-277

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 316-320

N-myristoylation sites.

amino acids 122-128, 125-131, 258-264

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 214-225

G-protein coupled receptors proteins.

amino acids 29-59, 76-116

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FIGURE 19

GCAAATGTGTGTGGCTGGAGGCGAGCCGAGGCTTTCGGCAAAGGCAGTCGAGTGTTTGCAGACCGGGGCGAGTC TTTCCAGCCAAGTGGACCTGATCGATGGCCCTCCTGAATTTATCACGATATTTGATTTATTAGCGATGCCCCCTG GTTTGTGTGTTACGCACACACACGTGCACACAGGCTCTGGCTCGCTTCCCTCGTTTCCAGCTCCTGGGCG ACGAGGGAAAAGAACCACAGACGCAACTTGAGACTCCCGCATCCCAAAAGAAGCACCAGATCAGCAAAA AAAGAAGATGGGCCCCCGAGCCTCGTGCTGTGCTTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTC GGCCTTCCTGTCGCACCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCCAACATCATCCT GGGCGGGCCCACTTCATCAACGCCTTCGTGACCACACCCATGTGCTGCCCCTCACGCTCCTCCATCCTCACTGG GAGCCGCACCTTTGCCGTGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAGTATCTTAATGAATA CAACGGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCGGACTCCTTAAAAAACTCCCGCTTTTATAACTACAC GCTGTGTCGGAACGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATTACCTCACAGACCTCATCACCAA TGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTTACCCGCACAGGCCAGTCCTCATGGTCATCAGCCATGC AGCCCCCCACGGCCCTGAGGATTCAGCCCCACAATATTCACGCCTCTTCCCAAACGCATCTCAGCACATCACGCC GAGCTACAACTACGCGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCATCACAT GGAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCTCATGTCGGTGGACGACTCCATGGAGACGATTTA CAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACACCGCCGACCACGGTTACCACATCGG $\verb|CCAGTTTGGCCTGGTGAAAGGGAAATCCATGCCATATGAGTTTGACATCAGGGTCCCGTTCTACGTGAGGGGCCC| \\$ ${\tt CAACGTGGAAGCCGGCTGTCTGAATCCCCACATCGTCCTCAACATTGACCTGGCCCCACCATCCTGGACATTGC}$ $\tt GTTTCACTTGAAAAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGGAGAGGGCAAGCTGCTACACAAGAG$ AGACAATGACAAGGTGGACGCCCAGGAGGAGAACTTTCTGCCCAAGTACCAGCGTGTGAAGGACCTGTGTCAGCG TGCTGAGTACCAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTGTGTGGAGGACGCCACGGGGAAGCTGAA GCTGCATAAGTGCAAGGGCCCCATGCGGCTGGGCGGCAGCAGAGCCCTCTCCAACCTCGTGCCCAAGTACTACGG GCAGGGCAGCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGGACGCCGGAAAAAACTCTT CAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCATCGAGGTGGACGGCAGGGT GTACCACGTAGGCCTGGGTGATGCCGCCCAGCCCCGAAACCTCACCAAGCGGCACTGGCCAGGGGCCCCTGAGGA CCAAGATGACAAGGATGGTGGGGACTTCAGTGGCACTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCCATTAA ${\tt AGTGACATCGGTGCTACATCCTAGAGAACGACACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGC}$ CTGGAAAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTGAGGGAAGT CCGAGGTCACCTGAAGAAAAAGCGGCCAGAAGAATGTGACTGTCACAAAATCAGCTACCACACCCCAGCACAAAGG CCGCCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTCAGGAAGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTT GCGGGAGCAGAAGCGCAAGAAGAAACTCCGCAAGCTGCTCAAGCGCCTGCAGAACAACGACACGTGCAGCATGCC AGGCCTCACGTGCTTCACCCACGACAACCAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGC CTGCACCAGCGCCAACAATAACACGTACTGGTGCATGAGGACCATCAATGAGACTCACAATTTCCTCTTCTGTGA ATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCAGCTGATGAATGCAGTGAACACACT GGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCATGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAA CCCCGGACTCGAAACATGGACCTGGATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCC $\tt AGAAATGAAGAGACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGT{\color{red}{\bf TAA}}{GAAACAACAGAGGT}$ GGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTGATTTCCAGCAGACC GCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTTGCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCAC AAAATGCATTTTTTCGTATCAAAAAGTCACCACTAACCCTCCCCCAGAAGCTCACAAAGGAAAACGGAGAGAGCG AGCGAGAGAGTTTCCTTGGAAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTTAAATCATAGGGGAAAAGCA GTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTCACAAAGAAGGAACTAAGAAGCAGGACAGAGGCAACGTGG AGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGCACAAAAGAGATGACATTTACCTAGCACTAT AAACCCTGGTTGCCTCTGAAGAAACTGCCTTCATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACT TTTAGGGGAACCTAATAAGAAATCCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAAA GAAAAA

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FIGURE 20

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRDRRNIRPNIILVLTDDQDVELGSMQV
MNKTRRIMEQGGAHFINAFVTTPMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHESRT
FAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSDYSK
DYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITPSYNY
APNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNTYIVYT
ADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDIAGLDIP
ADMDGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEENFLPKYQR
VKDLCQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKYYGQGSEAC
TCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAIEVDGRVYHVGLGDAAQPRNLTKRHW
PGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKSLQAWKDHKLH
IDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSLHPFRKGLQEKD
KVWLLREQKRKKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLGPFCACTSANNNT
YWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQLHVQLMELRSCKGY
KQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

Important features:

Signal peptide:

amino acids 1-17

Sulfatases signature 1.

amino acids 86-99

Homologous region to sulfatase:

amino acids 87-106, 133-146, 216-229, 291-320, 365-375

N-glycosylation sites.

amino acids 65-69, 112-116, 132-136, 149-153, 171-175, 198-202, 241-245, 561-565, 608-612, 717-721, 754-758, 764-768

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FIGURE 21

GGGCGCGAGAGCTGCTAGGGCGGTTTCTCTGCCTCGGGCCTGTTGGGCAGGGCCGGCT AAGGTGCGCGTGCTCGCTGGTTCTAACCCTTCTGTTGGGCGTTTCTGCTGAGAGGCGGGA GGCGCTGAGAGTCTGTGCGGAGGTCCGTGGACAGACTGCTTTGCTCGTTGTTGCTCTTCG GAGGCGGCGATCCCCGAAGGCGAGCTGAAATACGGCTGCAGGCTACAATTTGCAGCCGAC GATTATGGAAGACGGAAGCGGAGAGGTGGCCCACCCTC**ATG**GAGCGCTTGTGCTCGGAT GGCTTCGCATTCCCCAATACCCCATTAAACCGTATCATCTGAAGAGGATCCACAGAGCT GTCTTACATGGTAATCTAGAGAAACTGAAGTACCTTCTGCTCACGTATTATGACGCCAAT AAGAGAGACAGGAAGGAACGCCCCTACATTTGGCCTGTGCCACTGGCCAACCGGAA ATGGTACATCTCCTGGTGTCCAGAAGATGTGAGCTTAACCTCTGCGACCGTGAAGACAGG ACACCTCTGATCAAGGCTGTACAACTGAGGCAGGAGGCTTGTGCAACTCTTCTGCTGCAA AATGGCGCCAATCCAAATATTACGGATTTCTTTGGAAGGACTGCTCTGCACTACGCTGTG TATAATGAAGATACATCCATGATAGAAAAACTTCTTTCACATGGTACAAATATTGAAGAA ACATTGACACATGTAAGGGTCAATTTTTCATATTTGGAAGCTCAAACATTCCTTGAATGA AAATATTTTGAAATGCCTTAACTGTCTAAGATTTTACTTTAAATATTTGGAACTTTTAAAG AAGCATTATAGGGAACAGCCTTTTTTCATGCACTTATGGTAAATAACTATAAAAACAAAT GAATTACAATAAATTTATAATTCATGACAACTGAATTTGGGAAAGGTAATAGTTAAGTGT TTTTCCACTAAATTACTTTTT

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FIGURE 22

MERLCSDGFAFPQYPIKPYHLKRIHRAVLHGNLEKLKYLLLTYYDANKRDRKERTALHLACAT GQPEMVHLLVSRRCELNLCDREDRTPLIKAVQLRQEACATLLLQNGANPNITDFFGRTALHYA VYNEDTSMIEKLLSHGTNIEECSKV

Important features of the protein:

N-glycosylation site.

amino acids 113-117

N-myristoylation site.

amino acids 109-115

Microbodies C-terminal targeting signal.

amino acids 149-153

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FIGURE 23

GAGGCAGAAAGGCAGAAAGGAGAAAATTCAGGATAACTCTCCTGAGGGGTGAGCCAAGCCCTG CCATGTAGTGCACGCAGGACATCAACAAACACAGATAACAGGAAATGATCCATTCCCTGTGGT CACTTATTCTAAAGGCCCCAACCTTCAAAGTTCAAGTAGTGATATGGATGACTCCACAGAAAG GGAGCAGTCACGCCTTACTTCTTGCCTTAAGAAAAGAGAAAATGAAACTGAAGGAGTGTGT TTCCATCCTCCCACGGAAGGAAAGCCCCTCTGTCCGATCCTCCAAAGACGGAAAGCTGCTGGC TGCAACCTTGCTGCTGCACTGCTGTCTTGCTGCCTCACGGTGGTGTCTTTCTACCAGGTGGC CGCCTGCAAGGGGACCTGGCCAGCCTCCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCT GCCAGCAGGAGCAGGAGCCCCCAAGGCCGGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGACT GAAAATCTTTGAACCACCAGCTCCAGGAGAAGGCAACTCCAGTCAGAACAGCAGAAATAAGCG TGCCGTTCAGGGTCCAGAAGAACAGTCACTCAAGACTGCTTGCAACTGATTGCAGACAGTGA AACACCAACTATACAAAAAGGATCTTACACATTTGTTCCATGGCTTCTCAGCTTTAAAAAGGGG AAGTGCCCTAGAAGAAAAAGAGAATAAAATATTGGTCAAAGAAACTGGTTACTTTTTTATATA TGGTCAGGTTTTATATACTGATAAGACCTACGCCATGGGACATCTAATTCAGAGGAAGAAGGT CCATGTCTTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGATGTATTCAAAATATGCCTGA AACACTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAAAACTGGAAGAAGGAGATGAACT ${\tt TGCATTGAAACTGCTG}$

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FIGURE 24

MDDSTEREQSRLTSCLKKREEMKLKECVSILPRKESPSVRSSKDGKLLAATLLLALLSCCLTV VSFYQVAALQGDLASLRAELQGHHAEKLPAGAGAPKAGLEEAPAVTAGLKIFEPPAPGEGNSS QNSRNKRAVQGPEETVTQDCLQLIADSETPTIQKGSYTFVPWLLSFKRGSALEEKENKILVKE TGYFFIYGQVLYTDKTYAMGHLIQRKKVHVFGDELSLVTLFRCIQNMPETLPNNSCYSAGIAK LEEGDELQLAIPRENAQISLDGDVTFFGALKLL

Transmembrane domain:

amino acids 47-72

N-glycosylation site.

amino acids 124-127, 242-245

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 33-36, 173-176

N-myristoylation site.

amino acids 96-101

TNF family proteins.

amino acids 172-206

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FIGURE 25

CTGCTTGGATACCTCCAGTCCCCAAACTGTGTTCCAGGAGTTTTCTTGGCCGAAGCTGCCCGA TGTTTGAGCCTTTTCTTCCCAGAGAAGAAGATGGACTGAAAGCTGCCAGTTGGGGACTTTTTG TGATCACGGCGTTGCAGCGTTTTAAAGGAGGTGATGGGGCTTGCGCTGGCTTGTCTTCCCACC CAAGTGAAGAGTTGATGTTCACTGGTTATGCTTAGACAATGTGCAGTTTGTGTTAATTTAAAA TTTTGGGTGGGATAGGGCATAGGCTTGTGAAGGGCAGTCCGGATCCGGAGGAACTCGTCTTT GTCCCTGGTAGGAGAGACACCCCCAGTCTATCCTCGATGCCGTCAGCCTTGGCCATCTTCACT TGCCGCCCGAACTCGCACCCGTTTCAGGAGCGTCATGTCTACCTGGACGAGCCCATCAAAATC GGCCGCTCAGTGGCCCGCTGTCGACCAGCGCAGAATAATGCCACTTTTGATTGCAAAGTGCTA TCAAGGAACCACGCTCTCGTCTGGTTTGATCACAAGACGGGCAAGTTTTATCTTCAAGACACT AAAAGTAGTAATGGTACTTTTATAAATAGCCAGAGATTGAGTCGAGGCTCTGAAGAAAGTCCA CCATGTGAAATTCTTTCCGGTGACATTATCCAGTTTGGAGTAGACGTGACAGAGAATACACGG AAAGTTACCCATGGGTGTATTGTTTCCACAATAAAACTTTTTCTACCAGATGGTATGGAAGCC CGGCTCCGCTCAGATGTCATCCATGCACCATTACCAAGTCCTGTTGACAAAGTTGCTGCTAAC ACTCCAAGTATGTACTCTCAGGAACTATTCCAGCTTTCTCAGTATCTACAGGAGGCCTTACAT CGGGAACAAATGTTGGAACAGAAGTTAGCCACGCTTCAGCGGCTACTAGCCATCACCCAAGAG GCTTCAGATACCAGTTGGCAGGCTTTAATAGATGAAGATAGACTCTTATCACGGTTAGAAGTT ATGGGAAACCAATTACAGGCATGCTCCAAAAATCAAACAGAAGATAGTTTACGAAAGGAACTT ATAGCATTACAAGAGGATAAACATAACTATGAGACAACAGCCAAAGAGTCCCTGAGGCGGGTT CTTCAGGAGAAAATTGAAGTGGTTAGAAAACTTTCAGAAGTTGAGCGAAGTCTGAGTAATACT GAAGATGAATGTACCCATCTGAAAGAAATGAATGAAAGGACTCAGGAAGAATTAAGAGAATTA GCCAACAATATAATGGAGCAGTTAATGAGATTAAAGATTTATCTGATAAATTAAAGGTAGCA GAGGGAAAACAAGAGGAAATCCAACAGAAGGGACAGGCTGAGAAAAAAGAATTACAACATAAA ATAGATGAAATGGAAGAAAAAGAACAGGAGCTCCAGGCAAAAATAGAAGCTTTGCAAGCTGAT AATGATTTCACCAATGAAAGGCTAACAGCTTTACAAGTACGGTTAGAACATCTTCAGGAGAAA ACTCTTAAAGAATGCAGCAGCTTGGCTGATCGTCGAAGGGCATCTAACCAAAGCGGTAGAAGA $\texttt{AACAAAGCTTTCAAAAGGTTTGTTTTCTGTTTTTCTATGTTTTTTGACAGTTCTTTTGGA\\ \underline{\textbf{TAA}}$ TGAAGGTTAGTGTATATTTTCAAGGTTATAGTATTTTAACCATCAGTTTACTTCTTATAGCTC ACAAAATAGCAAGCCAGTAACAGTATCAGATAATATATAAAATAATCAGACTTCTGTTTTAAG AAGGGTATCGTAACTGGAATGTGTCTTTTTAAGTGGATGTATATTTATGGTTTTTTTGAATGTT AGTACTTGATATAGGTTTCTTTAGGTATTAAAGATTTGTTGCAATCTCTGTCATTCCCAGCAT TAATTTCAGCTTTGATCTCAAATTTTAATCAAACACAATGTAAGTCGTTTGTGATACAACTTA AGTGAAACATGCTTGCACTTCTATTTTGGGGGTTACAGTACCTTTAAAAATCTCTTATGATGTT TAATATTTCCTTAATTTTTGGCATCTCAGTTTGATTTAAACAAAATTAATGACTTTTGTGAAT GTAGAATCTTCTTATATTTTATGAGTAGTCCAGTAATTGCCCAAAGTAGTTTATTGTGTTAAT TCTGTTACAGTTGTCAGAGAAGAAAAGTGAGTTTTAAAGCACCATATTGTCAAGTCACTTTTA TACATAGGGAAATTAGGCAAATAAATTTGGTGGCATGTGTTTATCATAGTAGAACTTTCATTA GACTATACCAGTATAAAATTTAAAACTAGATTCACAGTCCTTTTGGCCAATTAAAACATTGAG TTACAAAAGTTTGAGATACTTAATTTTAGTACATTCTATTTTATTAAAGTAACTGGATTCATT TGACTTTTTTAACCATGTAAGAGGATGGTGTTATTTCAAATATCTCGTGGTTTCCATTCTGAA TTTTGTGCACGGCAGATGCCATATTTGGGGAAAAAATGCATAGAATATGCATCATTAATATTG TTTTGGCAAACAGGCATTGAGTTTCAGAACAGTGAACTATTTTTAGTACATATGGCAATTTTT TTCACCTTATTAAAGTGAGATGAGAACAGACCTTAAAATAGCTTTTACCTCACCATCCAAATA CCTATTCAGATTAGTTGGTTGAATAGCCAGCACTTTGAAGTAGAGCCTTAGG

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FIGURE 26

MEARLRSDVIHAPLPSPVDKVAANTPSMYSQELFQLSQYLQEALHREQMLEQKLATLQRLLAI TQEASDTSWQALIDEDRLLSRLEVMGNQLQACSKNQTEDSLRKELIALQEDKHNYETTAKESL RRVLQEKIEVVRKLSEVERSLSNTEDECTHLKEMNERTQEELRELANKYNGAVNEIKDLSDKL KVAEGKQEEIQQKGQAEKKELQHKIDEMEEKEQELQAKIEALQADNDFTNERLTALQVRLEHL QEKTLKECSSLADRRRASNQSGRRNKAFKRFVFCFSMFFDSSFG

Important features of the protein:

N-glycosylation sites.

amino acids 98-102, 271-275

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 138-142, 267-271

Amidation site.

amino acids 273-277

Tropomyosins proteins.

amino acids 169-217

FIGURE 27

GAACCTGGCGCCGCGGAACTGATCGCGGCCTAGTCCCGACGCGTGTGTGCTAGTGAGCCGGA GCCGGCGACGGCAGTGGCGGCCCGGCCTGCAGGAGCCCGACGGGGTCTCTGCCATGGGGG AGTGACGCGCCTGCACCCGCTGTTCCGCGGCAGCGGCGAGACATGAGGAGACCCCGCGACAGG GGCAGCGGCGGCTCGTGAGCCCCGGG**ATG**GAGGAGAAATACGGCGGGGACGTGCTGGCCG GCCCCGGCGGCGGCGGCCTTGGGCCGGTGGACGTACCCAGCGCTCGATTAACAAAATATA TTGTGTTACTATGTTTCACTAAATTTTTGAAGGCTGTGGGACTTTTCGAATCATATGATCTCC TAAAAGCTGTTCACATTGTTCAGTTCATTTTTATATTAAAACTTGGGACTGCATTTTTTATGG TTTTGTTTCAAAAGCCATTTTCTTCTGGGAAAACTATTACCAAACACCAGTGGATCAAAATAT TTAAACATGCAGTTGCTGGGTGTATTATTTCACTCTTGTGGTTTTTTTGGCCTCACTCTTTGTG GACCACTAAGGACTTTGCTGCTATTTGAGCACAGTGATATTGTTGTCATTTCACTACTCAGTG TTTTGTTCACCAGTTCTGGAGGAGGACCAGCAAAGACAAGGGGAGCTGCTTTTTTCATTATTG CTGTGATCTGTTTATTGCTTTTTGACAATGATCATCATGGCTAAAATGGCTGAACACCCTG AAGGACATCATGACAGTGCTCTAACTCATATGCTTTACACAGCCATTGCCTTCTTAGGTGTGG CAGATCACAAGGGTGGAGTATTATTGCTAGTACTGGCTTTGTGTTGTAAAGTTGGTTTTCATA CAGCTTCCAGAAAGCTCTCTGTCGACGTTGGTGGAGCTAAACGTCTTCAAGCTTTATCTCATC TGGAGTCTTGGTTTTCTCATTATGCCTTTTGCAACGGTTATCTTTTTTGTCATGATCCTGG ATTTCTACGTGGATTCCATTTGTTCAGTCAAAATGGAAGTTTCCAAATGTGCTCGTTATGGAT CCTTTCCCATTTTTATTAGTGCTCTCCTTTTTGGAAATTTTTTGGACACATCCAATAACAGACC AGCTTCGGGCTATGAACAAAGCAGCACCACGGGAGAGCACTGAACACGTCCTGTCTGGAGGAG TGGTAGTGAGTGCTATATTCTTCATTTTGTCTGCCAATATCTTATCATCTCCCTCTAAGAGAG GACAAAAAGGTACCCTTATTGGATATTCTCCTGAAGGAACACCTCTTTATAACTTCATGGGTG ATGCTTTTCAGCATAGCTCTCAATCGATCCCTAGGTTTATTAAGGAATCACTAAAACAAATTC TTGAGGAGAGTGACTCTAGGCAGATCTTTTACTTCTTGTGCTTGAATCTGCTTTTTACCTTTG TTTTTGACTGCTCTGCTTTAGTCATGGGACTTTTTGCTGCCCTGATGAGTAGGTGGAAAGCCA AATTAGACACTCACATGTTAACACCAGTCTCAGTTGGAGGGCTGATAGTAAACCTTATTGGTA TCTGTGCCTTTAGCCATGCCCATAGCCATGCCCATGGAGCTTCTCAAGGAAGCTGTCACTCAT CTGATCACAGCCATTCACACCATATGCATGGACACAGTGACCATGGGCATGGTCACAGCCACG GATCTGCGGGTGGAGGCATGAATGCTAACATGAGGGGTGTATTTCTACATGTTTTGGCAGATA CACTTGGCAGCATTGGTGTGATCGTATCCACAGTTCTTATAGAGCAGTTTGGATGGTTCATCG CTGACCCACTCTGTTCTTCTACTGCTATATTAATATTTCTCAGTGTTGTTCCACTGATTA AAGATGCCTGCCAGGTTCTACTCCTGAGATTGCCACCAGAATATGAAAAAGAACTACATATTG CTTTAGAAAAGATACAGAAAATTGAAGGATTAATATCATACCGAGACCCTCATTTTTGGCGTC ATTCTGCTAGTATTGTGGCAGGAACAATTCATATACAGGTGACATCTGATGTGCTAGAACAAA GAATAGTACAGCAGGTTACAGGAATACTTAAAGATGCTGGAGTAAACAATTTAACAATTCAAG TGGAAAAGGAGGCATACTTTCAACATATGTCTGGCCTAAGTACTGGATTTCATGATGTTCTGG CTATGACAAACAATGGAATCCATGAAATACTGCAAAGATGGTACTTACATCATG<u>TGA</u>GATA ACTCAAGAATTACCCCTGGAGAATAAACAATGAAGATTAAATGACTCAGTATTTGTAATATTG CCAGAAGGATAAAAATTACACATTAACTGTACAGAAACAGAGTTCCCTACTACTGGATCAAGG

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FIGURE 28

MEEKYGGDVLAGPGGGGGLGPVDVPSARLTKYIVLLCFTKFLKAVGLFESYDLLKAVHIVQFI FILKLGTAFFMVLFQKPFSSGKTITKHQWIKIFKHAVAGCIISLLWFFGLTLCGPLRTLLLFE HSDIVVISLLSVLFTSSGGGPAKTRGAAFFIIAVICLLLFDNDDLMAKMAEHPEGHHDSALTH MLYTAIAFLGVADHKGGVLLLVLALCCKVGFHTASRKLSVDVGGAKRLQALSHLVSVLLLCPW VIVLSVTTESKVESWFSLIMPFATVIFFVMILDFYVDSICSVKMEVSKCARYGSFPIFISALL FGNFWTHPITDQLRAMNKAAHQESTEHVLSGGVVVSAIFFILSANILSSPSKRGQKGTLIGYS PEGTPLYNFMGDAFQHSSQSIPRFIKESLKQILEESDSRQIFYFLCLNLLFTFVELFYGVLTN SLGLISDGFHMLFDCSALVMGLFAALMSRWKATRIFSYGYGRIEILSGFINGLFLIVIAFFVF MESVARLIDPPELDTHMLTPVSVGGLIVNLIGICAFSHAHSHAHGASQGSCHSSDHSHSHHMH GHSDHGHSHGSAGGGMNANMRGVFLHVLADTLGSIGVIVSTVLIEQFGWFIADPLCSLSTAILIFLSVVPLIKDACQVLLLRLPPEYEKELHIALEKIQKIEGLISYRDPHFWRHSASIVAGTIHQVTSDVLEQRIVQQVTGILKDAGVNNLTIQVEKEAYFQHMSGLSTGFHDVLAMTKQMESMKYCKDGTYIM

Important features of the protein:

Signal peptide:

amino acids 1-46

Transmembrane domains:

amino acids 59-77, 101-119, 150-167, 205-223, 239-258, 267-284, 305-324, 343-360, 421-440, 452-469, 486-505, 522-539, 592-612, 621-641

N-glycosylation site.

amino acids 721-725

Glycosaminoglycan attachment site.

amino acids 143-147

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 225-229

Tyrosine kinase phosphorylation sites.

amino acids 750-758, 756-764

N-myristoylation sites.

amino acids 14-20, 46-52, 102-108, 112-118, 144-150, 317-323, 347-353, 369-375, 372-378, 437-443, 462-468, 529-535, 549-555, 553-559, 579-585, 582-588, 583-589, 584-590, 605-611, 737-743

Multicopper oxidases protein:

amino acids 561-569

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FIGURE 29

GGCACGAGGGCAGGATATTAGAA**TT**GCTACTCCCCAGTCAATTTTCATCTTTGCAATCTGCA TTTTAATGATAACAGAATTAATTCTGGCCTCAAAAAGCTACTATGATATCTTAGGTGTGCCAA AATCGGCATCAGAGCGCCAAATCAAGAAGGCCTTTCACAAGTTGGCCATGAAGTACCACCCTG ACAAAAATAAGAGCCCGGATGCTGAAGCAAAATTCAGAGAGATTGCAGAAGCATATGAAACAC TCTCAGATGCTAATAGACGAAAAGAGTATGATACACTTGGACACAGTGCTTTTACTAGTGGTA AAGGACAAAGAGGTAGTGGAAGTTCTTTTGAGCAGTCATTTAACTTCAATTTTGATGACTTAT TTAAAGACTTTGGCTTTTTTGGTCAAAACCAAAACACTGGATCCAAGAAGCGTTTTGAAAATC ATTTCCAGACACGCCAGGATGGTGGTTCCAGTAGACAAAGGCATCATTTCCAAGAATTTTCTT TTGGAGGTGGATTATTTGATGACATGTTTGAAGATATGGAGAAAATGTTTTCTTTTAGTGGTT **AG**TTCTTATTCTCACTAAATCCAACTGGTTGACTCTTCCTCATTATCTTTGATGCTAA ACAATTTTCTGTGAACTATTTTGACAAGTGCATGATTTCACTTTAAACAATTTGATATAGCTA TTAAATATATTTAAGGGTTTTTTTTTTTGACAAATTCAACATTCAACGAGTAGACAAAATGCT AATTATTTCCCTGATTAGGAAAGTTTCTTTAAAAAACACGTAATTTTGCCTAGTGCTTTTTCT CTACCTGCCCTTGGGCTCACTAATATCACCAGTATTATTACCAAGAAAATATTGAGTTTACCT GATTAAACTTTAAAAGTTAATTGTAGATTTAAATTGTGTGAACCTAATGATTTTTGCAGTGAA ACCTTTACTAATTCAAAGTTGCATGTTCTATGACATCTGTGACTTGCGTTGCAGAGTGTACAT GAAACTGTATAATTGAGTCATTCAGTAAAGGAGAACAGTATCTTGGTTAATTGCTACTGAAAG GTTGAGAAAGGAATGGTTTGATATTTACCACAGCGCTGTGCCTTTCTACAGTAGAACTGGGGT AAAGGAAATGGTTTTATTGCCCATAGTCATTTAGGCTGGAAAAAAGTTGAAAACTTAACGAAA TATTGCCAAGAGATTGTTATGTGTTTGGTTCCAGCCTAAAAATGATTTTGTAGTGTTGAAAATC ATAGCTACTTACATAGCTTTTTCATATTTCTTTCTTAGTTGTTGGCACTCTTAGGTCTTAGTA GATACCTCATTCTGTTAAAACCAGCCAGTAATTTCTGTGCAACCTTACTATGTGCAATAT TTTTAAATCCTGAGAAATGTGTGCTTTTGTTTTCGGATAGACTTATTTCTTTAGTTCTGCACT TTTCCACATTATACTCCATATGAGTATTAATCCTATGGATACATATTAAAACAAGTGTCTCAT

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FIGURE 30

MATPQSIFIFAICILMITELILASKSYYDILGVPKSASERQIKKAFHKLAMKYHPDKNKSPDA EAKFREIAEAYETLSDANRRKEYDTLGHSAFTSGKGQRGSGSSFEQSFNFNFDDLFKDFGFFG QNQNTGSKKRFENHFQTRQDGGSSRQRHHFQEFSFGGGLFDDMFEDMEKMFSFSGFDSTNQHT VQTENRFHGSSKHCRTVTQRRGNMVTTYTDCSGQ

Important features of the protein:

Signal peptide:

amino acids 1-23

Nt-dnaJ domain signature.

amino acids 27-59, 66-90

Glycosaminoglycan attachment site.

amino acids 96-100

N-myristoylation sites.

amino acids 32-38, 99-105, 102-108, 126-132, 211-217

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FIGURE 31

AAAGTTACATTTTCTCTGGAACTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTGG GCAGAAAGGAGGGTGCTTCGGAGCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACAAT ATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACTGAGTCTACCAAATG CAGACTTTCACAATGGTTCTAGAAGAATCTGGACAAGTCTTTTCATGTGGTTTTTCTACGCA CTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGAAACAGTG TACTATTCTGTCGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCTGGATCCCC AGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATCACGGCCACT GTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTGGAGCATCCTG AAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGATCACCAAAGAT GGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTCCTTGTGGCCTAC TGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGGGGGTATTCCAGTG CACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGACATTCGTGAAGGCC ATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAAGGAGAGGCCATTCCC CTGGTACTGGCCCTGTTTGCCTTTGTTGGCTTCATGCTGATCCTTGTGGTCGTGCCACTGTTC GTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGGTGGTCCTCCCAGACACC TTGAAAATAACCAATTCACCCCAGAAGTTAATCAGCTGCAGAAGGGAGGAGGTGGATGCCTGT ${\tt GCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGATCTCA} {\color{red}{\bf TAG}} {\tt GTTTGCGGAAGG}$ GCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACCATGAGGGGACAAGTTGTGTT TCTGTTTTCCGCCACGGACAAGGGATGAGAAGTAGGAAGAGCCTGTTGTCTACAAGTCTAG ACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACCCTGGGAAAAGTGACTTCATCCCT ACAGAGTCTCTCTATATATACACACGTACACATAAATACACCCAGCACTTGCAAGGCTAGA GGGAAACTGGTGACACTCTACAGTCTGACTGATTCAGTGTTTCTGGAGAGCAGGACATAAATG TATGATGAGAATGATCAAGGACTCTACACACTGGGTGGCTTGGAGAGCCCACTTTCCCAGAAT AATCCTTGAGAGAAAAGGAATCATGGGAGCAATGGTGTTGAGTTCACTTCAAGCCCAATGCCG GTGCAGAGGGGAATGGCTTAGCGAGCTCTACAGTAGGTGACCTGGAGGAAGGTCACAGCCACA CTGAAAATGGGATGTGCATGAACACGGAGGATCCATGAACTACTGTAAAGTGTTGACAGTGTG TGCACACTGCAGACAGCAGGTGAAATGTATGTGTGCAATGCGACGAGAATGCAGAAGTCAGTA ACATGTGCATGTTTGTTGTGCTCCTTTTTTCTGTTGGTAAAGTACAGAATTCAGCAAATAAAA

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FIGURE 32

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGET
VYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSI
LKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSGGIP
VHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILVVVPL
FVWKMGRLLOYSCCPVVVLPDTLKITNSPOKLISCRREEVDACATAVMSPEELLRAWIS

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 230-255

N-glycosylation sites.

amino acids 40-44, 134-138

Tissue factor proteins.

amino acids 92-120

Integrins alpha chain proteins.

amino acids 232-263

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FIGURE 33

GAGACACGCGAGCGGGGAGACCTCCAAGGCAGCGAGGCATCGGACATGTGTCAGCACATCTGG GGCGCACATCCGTCGAGCCCGAGGGGAGATTTGCCGGAACAATTCAAACTGCGATATTGATCT GTGATGCACTTGGAATGAGAATCAGAGGATGGAAATAGTCTGGGAGGTGCTTTTTCTTCTTCA AGCCAATTTCATCGTCTGCATATCAGCTCAACAGAATTCACCAAAAATCCATGAAGGCTGGTG CTCAGCTTGGAATCTTTGCTCTGTGGGGAAACGGCAGTCGCCAGTCAACATAGAGACCAGTCA CATGATCTTCGACCCCTTTCTGACACCTCTTCGCATCAACACGGGGGGCAGGAAGGTCAGTGG GACCATGTACAACACTGGAAGACACGTATCCCTTCGCCTGGACAAGGAGCACTTGGTCAACAT ATCTGGAGGGCCCATGACATACAGCCACCGGCTGGAGGAGATCCGACTACACTTTGGGAGTGA GGACAGCCAAGGGTCGGAGCACCTCCTCAATGGACAGGCCTTCTCTGGGGAGGTGCAGCTCAT CCACTATAACCATGAGCTATATACGAATGTCACAGAAGCTGCAAAGAGTCCAAATGGATTGGT GGTAGTTTCTATATTATAAAAGTTTCTGATTCATCAAACCCATTTCTTAATCGAATGCTCAA CAGAGATACTATCACAAGAATAACATATAAAAATGATGCATATTTACTACAGGGGCTTAATAT AGAGGAACTATATCCAGAGACCTCTAGTTTCATCACTTACGATGGGTCGATGACTATCCCACC CTGCTATGAGACAGCAAGTTGGATCATAATGAACAAACCTGTCTATATAACCAGGATGCAGAT GCATTCCTTGCGCCTGCTCAGCCAGAACCAGCCATCTCAGATCTTTCTGAGCATGAGTGACAA CTTCAGGCCTGTCCAGCCACTCAACAACCGCTGCATCCGCACCAATATCAACTTCAGTTTACA CAAG<u>TAG</u>GGAACAAAGCCAAGAAGAATCCCACCTCAGTGAAATGCTACAACTGTGAATTGACG GGGATTGGCCCTTTCTTCATGAAAAGTGTCTGCGAAACCATGGCAGAGGAATACATCTCTCAC CACACACACTCTCTTACAACCTCCATCATGGGAAGTCAAGTTTCAGAAACAAAAGTCTCAT TCATAAGAGGTCTTAGAAGAAAATAACCAGTTAACCTGATTTCAATTTTGATACCGTTTTCCT GAGAGGAGAAAATACAGCTCTGATGGCATCAAACGGACTTTGCATCAAGTAATTTCAGATAGT GTCCTAGGATCCTTTGAGGGTGCTGGTAGCAGGTGAGCAGGACAAAGTTGACCAAGGACACTT AAGAGCTACACATTGTATATATCACCACAGACTATAAGGAAATGGAATTATTTCCCTCTTT GTCACATATCTGTAGTAGGATTTGCCAAGATCAGAAATGATCCATTTGCTGTTTCTTGTTTTC CAAAGGTCATACATTGTGTTTGGTTATTGTTACCAGCTCAATAAATGTGTTTAACGAGTTAAT TTCATTTTTCTGGCTTTGGTCTGTTCTCCTTCCTTACAGGCTAAGCCCTGGCTCCATGCAACT GCATTCTTTGATTTCACTTGTTCCTTCATCTACATGTTTTGTTCATTTGCAGCCAGTTTTTAC TGAGTTTGTGGCAATCAGGAATGCATTTGCTAAGCAAGTATGACTTTAATTCCACTCCATGGC TCAATCATTCACATGAGGTGAGCTTCAGCCTGAGATAGCAGGCGACAGACTTCTTGCGTTTCA AAACTGCCATGCCCCCTGTGATGCTCCCGTGAAGGAATGCACTTTGCCTTGTAAGTTCCTGG GAAAGGGGTATGTTTTCTCTCCAGGTGCAGCCAGATCTCACAAAGTACAAAACGAATGCCTTT CTTTTCTTGTTTATAATGGTCACTCACTGTGTTTTGGTTACTGTCAAGAAATCAATAAATGTGT TTAACAAGTTA

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FIGURE 34

MEIVWEVLFLLQANFIVCISAQQNSPKIHEGWWAYKEVVQGSFVPVPSFWGLVNSAWNLCSVG KRQSPVNIETSHMIFDPFLTPLRINTGGRKVSGTMYNTGRHVSLRLDKEHLVNISGGPMTYSH RLEEIRLHFGSEDSQGSEHLLNGQAFSGEVQLIHYNHELYTNVTEAAKSPNGLVVVSIFIKVS DSSNPFLNRMLNRDTITRITYKNDAYLLQGLNIEELYPETSSFITYDGSMTIPPCYETASWII MNKPVYITRMQMHSLRLLSQNQPSQIFLSMSDNFRPVQPLNNRCIRTNINFSLQGKDCPNNRA QKLQYRVNEWLLK

Important features:

Signal peptide:

amino acids 1-20

Eukaryotic-type carbonic anhydrases proteins.

amino acids 126-162, 220-269, 43-91

N-glycosylation sites.

amino acids 116-119, 168-171, 302-305

FIGURE 35

GTCGGAACCCCTCAGGCCACCCTCGGGAGTCCTGGGGTCCAGAGGGGTGTCCCTGTACCCCTTGCAC ACAGGACCCTCACTCTGCAGGGATAAGCCAGCTGCGCCTGCAGCCTAGGGTGCCAAGGAGGCTGCTGA TTGTGGCCCACAGCCTCATCTGAACGCCAGGAGACCAGGATACCGAGGCACCGGATCCCCTCTGTG CCCTGGGGAGCCCCAGTGCTGCCCAGTCACCCCAGGGCTGAGGTCTGCGTCCCTAGTGGTGCAAGGCC TGGTAGGACCACGGGGCAGGGAATGTGAGCGCCATCCGAGCTCACGGTGTCCTGAGTCGCGGCTTCGT GACTTTGGCAGGGGCCTCCGGACCAGTGACCCCAGTCAAACCCAGAGGGTCTTGGGCGGCAGCGACGA AGGAGGTATTCAGGCTCCAGGCCAGGTGGGGCCGGACGCCCCCAGCCATCCACC<u>ATG</u>GTGGTGGCACA CCCCACCGCCACTGCCACCACCACCGCCCACTGCCACTGTCACGGCCACCGTTGTGATGACCACGGCCA CCATGGACCTGCGGGACTGGCTGTTCCTCTGCTACGGGCTCATCGCCTTCCTGACGGAGGTCATCGAC ATCCATCCCGCAGATATCCCTGATGACGCCACCACCCTCTACCTGCAGAACAACCAGATCAACAACG CCGGCATCCCCCAGGACCTCAAGACCAAGGTCAACGTGCAGGTCATCTACCTATACGAGAATGACCTG GATGAGTTCCCCATCAACCTGCCCCGCTCCCTCCGGGAGCTGCACCTGCAGGACAACAATGTGCGCAC CATTGCCAGGGACTCGCTGGCCCGCATCCCGCTGCTGGAGAAGCTGCACCTGGATGACAACTCCGTGT CCACCGTCAGCATTGAGGAGGACGCCTTCGCCGACAGCAAACAGCTCAAGCTGCTCTTCCTGAGCCGG AACCACCTGAGCAGCATCCCCTCGGGGCTGCCGCACACGCTGGAGGAGCTGCGGCTGGATGACAACCG CATCTCCACCATCCCGCTGCATGCCTTCAAGGGCCTCAACAGCCTGCGGCGCCTGGTGCTGGACGGTA ACCTGCTGGCCAACCAGCGCATCGCCGACGACACCTTCAGCCGCCTACAGAACCTCACAGAGCTCTCG CTGGTGCGCAATTCGCTGGCCGCGCCACCCTCAACCTGCCCAGCGCCCACCTGCAGAAGCTCTACCT GCAGGACAATGCCATCAGCCACATCCCCTACAACACGCTGGCCAAGATGCGTGAGCTGGAGCGGCTGG ACCTGTCCAACAACACCTGACCACGCTGCCCCGCGGCCTGTTCGACGACCTGGGGAACCTGGCCCAG CTGCTGCTCAGGAACACCCTTGGTTTTGTGGCTGCAACCTCATGTGGCTGCGGGACTGGGTGAAGGC ACGGGCGGCCGTGGTCAACGTGCGGGGCCTCATGTGCCAGGGCCCTGAGAAGGTCCGGGGCATGGCCA TCAAGGACATTACCAGCGAGATGGACGAGTGTTTTGAGACGGGGCCGCAGGGCGGCGTGGCCAATGCG GCTGCCAAGACCACGGCCAGCAACCACGCCTCTGCCACCACGCCCCAGGGTTCCCTGTTTACCCTCAA GGCCAAAAGGCCAGGGCTGCGCCTCCCCGACTCCAACATTGACTACCCCATGGCCACGGGTGATGGCG CCAAGACCCTGGCCATCCACGTGAAGGCCCTGACGGCAGACTCCATCCGCATCACGTGGAAGGCCACG CTCCCCGCCTCCTCTTTCCGGCTCAGTTGGCTGCGCCTGGGCCACAGCCCAGCCGTGGGCTCCATCAC GGAGACCTTGGTGCAGGGGGACAAGACAGAGTACCTGCTGACAGCCCTGGAGCCCAAGTCCACCTACA TCATCTGCATGGTCACCATGGAGACCAGCAATGCCTATGTAGCTGATGAGACACCCGTGTGTGCCAAG GAGCCTGCCCTGGCGGGCATCATCGGCGGGGCAGTGGCTCTGGTCTTCCTCTTCCTGGTCCTGGGGG CCATCTGCTGGTACGTGCACCAGGCTGGCGAGCTGCTGACCCGGGAGAGGGCCTACAACCGGGGCAGC AGGAAAAAGGATGACTATATGGAGTCAGGGACCAAGAAGGATAACTCCATCCTGGAAATCCGCGGCCC TGGGCTGCAGATGCTGCCCATCAACCCGTACCGCGCCAAAGAGGAGTACGTGGTCCACACTATCTTCC CCTCCAACGGCAGCAGCCTCTGCAAGGCCACACACACCATTGGCTACGGCACCACGCGGGGCTACCGG GACGGCGGCATCCCGACATAGACTACTCCTACACA<u>TGA</u>TGCCCGCCCACCCGGGCTGCCCCGCCTCA GCCCCAGCTGCCCTGGCGTGGCCATGTGGCTTTGCCCAGCCTGCTGCAATCCAAGAGAGCAAGGAAGA GAAATTCCATGGGTGACTTTCCTCCGCAGAAAGCAAAGTTTGGGGAGGGCTGACGATTTTGTAGAACA CAACAGTGACAATTTTTTTTAAAAGAATAGAAGGCAGGAGGGGGGAATTCGACATTGTTGAAGACATAA GTTTTTTTTTTCCCCCCTGAACTGGAAGGATACTACCTGTACAACATCTGTGGACACCTCATGCTCT GTTCAAGGCCATCACAAAGGAACCGCCAGGGAGAAGCAGCCGGCTCTCAAAGCTCCCACGCAGCTCTC CCGCCACTGGCCACTCGCTGGCGACCCGATGGAAGGTTTTCAGGCTCCTCACAAAGGAGAGAGGGAAG AAAAGATCTTTTGCCCTGGAGATATGGTCCTGAAATCTCTCCCCTGGCTTATTCCATACCATTTCCCT TGCAGATTTGCAGAAACATGGCATCTTTCACTGCATTCTTTGAACAATCATGTAGTCGATTAAAAAAA AAAACAAACTTTTTTTCCTAGGCTGAAGCCCTCTTCAGTTCCATGCACCACGCTCCGTAGAAGCCCC TCTCTAAGTACAGATGGGTAGATAGAGCCACATGCACGGTCCTTACCGTTCTTCTTGGGTCAGTTCTT ACCATTTCCTGAACAATAGAATTGTGAAAGTGTTAAAAA

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FIGURE 36

MVVAHPTATATTTPTATVTATVVMTTATMDLRDWLFLCYGLIAFLTEVIDSTTCPSVCRCDNG
FIYCNDRGLTSIPADIPDDATTLYLQNNQINNAGIPQDLKTKVNVQVIYLYENDLDEFPINLP
RSLRELHLQDNNVRTIARDSLARIPLLEKLHLDDNSVSTVSIEEDÄFADSKQLKLLFLSRNHL
SSIPSGLPHTLEELRLDDNRISTIPLHAFKGLNSLRRLVLDGNLLANQRIADDTFSRLQNLTE
LSLVRNSLAAPPLNLPSAHLQKLYLQDNAISHIPYNTLAKMRELERLDLSNNNLTTLPRGLFD
DLGNLAQLLLRNNPWFCGCNLMWLRDWVKARAAVVNVRGLMCQGPEKVRGMAIKDITSEMDEC
FETGPQGGVANAAAKTTASNHASATTPQGSLFTLKAKRPGLRLPDSNIDYPMATGDGAKTLAI
HVKALTADSIRITWKATLPASSFRLSWLRLGHSPAVGSITETLVQGDKTEYLLTALEPKSTYI
ICMVTMETSNAYVADETPVCAKAETADSYGPTTTLNQEQNAGPMASLPLAGIIGGAVALVFLF
LVLGAICWYVHQAGELLTRERAYNRGSRKKDDYMESGTKKDNSILEIRGPGLQMLPINPYRAK
EEYVVHTIFPSNGSSLCKATHTIGYGTTRGYRDGGIPDIDYSYT

Important features of the protein:

Transmembrane domain:

amino acids 552-573

N-glycosylation sites.

amino acids 249-252, 305-308, 642-645

Leucine zipper pattern.

amino acids 182-203, 299-320

Phospholipase A2 aspartic acid active site.

amino acids 57-67

FIGURE 37

GGTGACTGAAGCGAGCCTGGCCTCTTGCATCCTCCGCCTGTGTACCTCCCCTTCTCTTTTTTCCGCCT CTGAGCCTGGGCACAGCCACCATCTCTCCGCCAGAGTCAGGAGAGAACTGAGAGGCGCATACCCCGG CTGTGGCGGCTGCTCTGGGCTGGGACCGCCTTCCAGGTGACCCAGGGAACGGGACCGGAGCTTCA TGCCTGCAAAGAGTCTGAGTACCACTATGAGTACACGGCGTGTGACAGCACGGGTTCCAGGTGGAGGG TCGCCGTGCCGCATACCCCGGGCCTGTGCACCAGCCTGTCTGACCCCGTCAAGGGCACCGAGTGCTCC TTCTCCTGCAACGCCGGGGAGTTTCTGGATATGAAGGACCAGTCATGTAAGCCATGCGCTGAGGGCCG CTACTCCCTCGGCACAGGCATTCGGTTTGATGAGTGGGGATGAGCTGCCCCATGGCTTTGCCAGCCTCT CAGCCAACATGGAGCTGGATGACAGTGCTGCTGAGTCCACCGGGAACTGTACTTCGTCCAAGTGGGTT CCCCGGGGCGACTACATCGCCTCCAACACGGACGAATGCACAGCCACACTGATGTACGCCGTCAACCT GAAGCAATCTGGCACCGTTAACTTCGAATACTACTATCCAGACTCCAGCATCATCTTTGAGTTTTTCG TTCAGAATGACCAGTGCCAGCCCAATGCAGATGACTCCAGGTGGATGAAGACCACAGAGAAAAGGATGG GAATTCCACAGTGTGGAGCTAAATCGAGGCAATAATGTCCTCTATTGGAGAACCACAGCCTTCTCAGT ATGGACCAAAGTACCCAAGCCTGTGCTGGTGAGAAACATTGCCATAACAGGGGTGGCCTACACTTCAG AATGCTTCCCCTGCAAACCTGGCACGTATGCAGACAAGCAGGGCTCCTCTTTCTGCAAACTTTGCCCA GCCAACTCTTATTCAAATAAAGGAGAAACTTCTTGCCACCAGTGTGACCCTGACAAATACTCAGAGAA GCGATGCCAACGGAGAGACACACTCATGTACAAATGGGCCAAGCCGAAAATCTGTAGCGAGGACCTT GAGGGGGCAGTGAAGCTGCCTGCCTCTGGTGTGAAGACCCACTGCCCACCCTGCAACCCAGGCTTCTT CAAAACCAACAGCACCTGCCAGCCCTGCCCATATGGTTCCTACTCCAATGGCTCAGACTGTACCC GCTGCCCTGCAGGGACTGAACCTGCTGTGGGATTTGAATACAAATGGTGGAACACGCTGCCCACAAAC ATGGAAACGACCGTTCTCAGTGGGATCAACTTCGAGTACAAGGGCATGACAGGCTGGGAGGTGGCTGG TGATCACATTTACACAGCTGCTGGAGCCTCAGACAATGACTTCATGATTCTCACTCTGGTTGTGCCAG GATTTAGACCTCCGCAGTCGGTGATGGCAGACACAGAGAATAAAGAGGTGGCCAGAATCACATTTGTC TCCTGTGGAGACGTGGAAAGGTTCCAAAGGCAAACAGTCCTATACCTACATCATTGAGGAGAACACTA CCACGAGCTTCACCTGGGCCTTCCAGAGGACCACTTTTCATGAGGCAAGCAGGAAGTACACCAATGAC GTTGCCAAGATCTACTCCATCAATGTCACCAATGTTATGAATGGCGTGGCCTCCTACTGCCGTCCCTG TGCCCTAGAAGCCTCTGATGTGGGCTCCTCCTGCACCTCTTGTCCTGCTGGTTACTATATTGACCGAG ATTCAGGAACCTGCCACTCCTGCCCCCCTAACACAATTCTGAAAGCCCACCAGCCTTATGGTGTCCAG GCCTGTGTGCCCTGTGGTCCAGGGACCAAGAACAACAAGATCCACTCTCTGTGCTACAATGATTGCAC CTTCTCACGCAACACTCCAACCAGGACTTTCAACTACAACTTCTCCGCTTTGGCAAACACCGTCACTC TTGCTGGAGGGCCAAGCTTCACTTCCAAAGGGTTGAAATACTTCCATCACTTTACCCTCAGTCTCTGT GGAAACCAGGGTAGGAAAATGTCTGTGTGCACCGACAATGTCACTGACCTCCGGATTCCTGAGGGTGA GTCAGGGTTCTCCAAATCTATCACAGCCTACGTCTGCCAGGCAGTCATCATCCCCCCAGAGGTGACAG GCTACAAGGCCGGGGTTTCCTCACAGCCTGTCAGCCTTGCTGATCGACTTATTGGGGTGACAACAGAT ATGACTCTGGATGGAATCACCTCCCCAGCTGAACTTTTCCACCTGGAGTCCTTGGGAATACCGGACGT GATCTTCTTTTATAGGTCCAATGATGTGACCCAGTCCTGCAGTTCTGGGAGATCAACCACCATCCGCG TCAGGTGCAGTCCACAGAAAACTGTCCCTGGAAGTTTGCTGCTGCCAGGAACGTGCTCAGATGGGACC TGTGATGGCTGCAACTTCCACTTCCTGTGGGAGAGCGCGGCTGCTTGCCCGGCTCTGCTCAGTGGCTGA CTACCATGCTATCGTCAGCAGCTGTGTGGCTGGGATCCAGANGACTACTTACGTGTGNCGAGAACCCA AGCTATGCTCTGGTGGCATTTCTCTGCCTGAGCAGAGAGTCACCATCTGCAAAACCATAGATTTCTGG CTGAAAGTGGGCATCTCTGCAGGCACCTGTACTGCCATCCTGCTCACCGTCTTGACCTGCTACTTTTG GAAAAAGAATCAAAAACTAGAGTACAAGTACTCCAAGCTGGTGATGAATGCTACTCTCAAGGACTGTG ACCTGCCAGCAGCTGACAGCTGCGCCATCATGGAAGGCGAGGATGTAGAGGACGACCTCATCTTTACC AGCAAGAAGTCACTTTTTGGGAAGATCAAATCATTTACCTCCAAGAGGACTCCTGATGGATTTGACTC AGTGCCGCTGAAGACATCCTCAGGAGGCCCAGACATGGACCTG<u>TGA</u>GAGGCACTGCCTGCCTCACCTG CCTCCTCACCTTGCATAGCACCTTTGCAAGCCTGCGGCGATTTGGGTGCCAGCATCCTGCAACACCCA $\tt CTGCTGGAAATCTCTTCATTGTGGCCTTATCAGATGTTTGAATTTCAGATCTTTTTTTATAGAGTACC$

FIGURE 38

MAEPGHSHHLSARVRRRTERRIPRLWRLLLWAGTAFOVTOGTGPELHACKESEYHYEYTACDS TGSRWRVAVPHTPGLCTSLSDPVKGTECSFSCNAGEFLDMKDQSCKPCAEGRYSLGTGIRFDE WDELPHGFASLSANMELDDSAAESTGNCTSSKWVPRGDYIASNTDECTATLMYAVNLKQSGTV NFEYYYPDSSIIFEFFVONDOCOPNADDSRWMKTTEKGWEFHSVELNRGNNVLYWRTTAFSVW TKVPKPVLVRNIAITGVAYTSECFPCKPGTYADKQGSSFCKLCPANSYSNKGETSCHQCDPDK YSEKGSSSCNVRPACTDKDYFYTHTACDANGETOLMYKWAKPKICSEDLEGAVKLPASGVKTH CPPCNPGFFKTNNSTCQPCPYGSYSNGSDCTRCPAGTEPAVGFEYKWWNTLPTNMETTVLSGI NFEYKGMTGWEVAGDHIYTAAGASDNDFMILTLVVPGFRPPQSVMADTENKEVARITFVFETL CSVNCELYFMVGVNSRTNTPVETWKGSKGKQSYTYIIEENTTTSFTWAFQRTTFHEASRKYTN DVAKIYSINVTNVMNGVASYCRPCALEASDVGSSCTSCPAGYYIDRDSGTCHSCPPNTILKAH QPYGVQACVPCGPGTKNNKIHSLCYNDCTFSRNTPTRTFNYNFSALANTVTLAGGPSFTSKGL KYFHHFTLSLCGNQGRKMSVCTDNVTDLRIPEGESGFSKSITAYVCQAVIIPPEVTGYKAGVS SQPVSLADRLIGVTTDMTLDGITSPAELFHLESLGIPDVIFFYRSNDVTQSCSSGRSTTIRVR CSPQKTVPGSLLLPGTCSDGTCDGCNFHFLWESAAACPLCSVADYHAIVSSCVAGIQXTTYVX REPKLCSGGISLPEORVTICKTIDFWLKVGISAGTCTAILLTVLTCYFWKKNQKLEYKYSKLV MNATLKDCDLPAADSCAIMEGEDVEDDLIFTSKKSLFGKIKSFTSKRTPDGFDSVPLKTSSGG PDMDL

Important features of the protein:

N-glycosylation sites:

amino acids 153-156, 390-393, 391-394, 404-407, 544-547, 576-579, 672-675, 717-720, 947-950

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

amino acids 15-18, 563-566, 709-712

Casein kinase II phosphorylation sites:

amino acids 42-45, 59-62, 81-84, 146-149, 168-171, 282-285, 331-334, 340-343, 431-434, 449-452, 465-468, 523-526, 557-560, 761-764, 780-783, 835-838, 860-863, 893-896, 949-952

Tyrosine kinase phosphorylation sites:

amino acids 50-56, 109-116

N-myristoylation sites:

amino acids 77-82, 88-93, 152-157, 268-273, 288-293, 320-325, 400-405, 405-410, 414-419, 463-468, 599-604, 616-621, 634-639, 644-649, 839-844, 874-879, 912-917, 916-921

Amidation site:

amino acids 707-710

Cell attachment sequence:

amino acids 162-164

FIGURE 39

GGGAAGGGTTCTGGGCTGCCGCAGGCACACAGGCCAGAGCTTCGTGGATACCTGCAGGGCCC AAAGGTCCCTCCTGTTTTGAAGAGTGAGTGATGGCTATGAGGTAGCGGCCAGGCTGATCACC CCTGCGTTGGCTGGAGGCAGAATTCTGTAAATCCTCGCCAAGTCTTTCTCCAGGCCACTGGTT AGCTCATCTCAGCCTCCTCTGGGAGCATCAACACCAACATGGCACAGGGGACTGCAGTGGTGT GCTTTGGACCTGTGTACCCACCCAAGGCTAAAGGCAGAGCCAGGTGACTTTGCGGGGGTCTCT ACCCACCTTCTTCATGAGAACCACACTAAATTGCAAAAATTATCCCAGTGCTGGAGGAGGGC CTGCTTTGTGCTTTAAAGGAGCCAAGTTACACCCTGTTTAACCCTGCCTTCAAAGGGACGACT CTGTAAGATTCTCTGCTACTTATTCAAGTTGACACG<u>ATG</u>CCCTTCACACTCCACCTGAGGTCC CGCCTTCCCTCTGCCATAAGGAGTTTGATTCTACAAAAGAAACCAAACATCAGAAATACATCC AGCATGGCTGGAGAGCTCCGACCAGCCTGGTGGTCCTGCCCAGGTCCCTTGCTCCAGCT TTTGAAAGATTCTGCCAGGTCAACACTGGTCCTCTACCCCTGCTGGGCCAGAGTGAGCCAGAA AAGTGGATGCTGCCCCCTCAAGGTGCTATCTCAGAGACCAGGATGGGCCATCCCCAGTTCTGG AAATACGAGTTCGGTGCCTGCACCGGTAGCCTGGCTTCGCTGGAGCAGTACTCGGAGCAGCTG AAGGACATGGTGGCCTTCTTCCTGGGCTGCAGCTTCTCCCTGGAGGAGGCCTTGGAGAAAGCG GGGCTCCCCAGAAGAGACCCAGCAGGTCACAGCCAGGCGGGTGCATACAAGACAACAGTGCCT TGTGTTACCCATGCTGGCTTCTGCTGCCCTCTGGTGGTCACGATGAGGCCCATTCCCAAGGAC AAGCTGGAAGGGCTGGTGCGGGCCTGCTCCCTCGGAGGTGAGCAGGGGCAACCTGTTCAC ATGGGCGACCCAGAACTGTTGGGAATCAAAGAGCTTTCCAAACCTGCCTACGGGGATGCCATG GTGTGTCCCCCAGGGGAGGTTCCAGTGTTCTGGCCTTCTCCGCTGACCAGTCTCGGAGCTGTC AAGGATGCAAAGGCTCCACCTGGTTGTCTCACCCCAGAGAGAATTCCAGAGGTCCATCACATT TCCCAAGATCCTCTGCACTACAGCATCGCGTCAGTCTCTGCTTCTCAGAAGATCAGAGAACTA GAGTCTATGATCGGCATAGACCCAGGGAACCGGGGGATTGGGCACCTGCTCTGTAAAGATGAG CTGCTGAAGGCCTCTCTCTCGCTGTCCCATGCCCGCTCAGTGCTCATCACCACTGGGTTCCCC ACACATTTCAATCATGAGCCTCCAGAAGAGACAGATGGCCCACCAGGAGCTGTTGCTCTGGTT GCCTTCCTGCAGGCCTTGGAGAAGGAGGTCGCCATAATCGTTGACCAGAGAGCCTGGAACTTG CACCAGAAGATTGTTGAAGATGCTGTTGAGCAAGGTGTTCTGAAGACGCAGATCCCGATATTA ACTTACCAAGGTGGATCAGTGGAAGCTGCTCAGGCATTCCTGTGCAAAAATGGGGACCCGCAG ACACCTAGATTTGACCACCTGGTGGCCATAGAGCGTGCCGGAAGAGCTGCTGATGGCAATTAC TACAATGCAAGGAAGATGAACATCAAGCACTTGGTTGACCCCATTGACGATCTTTTTCTTGCT GCGAAGAAGATTCCTGGAATCTCATCAACTGGAGTCGGTGATGGAGGCAACGAGCTTGGGATG GGTAAAGTCAAGGAGGCTGTGAGGAGGCACATACGGCACGGGGATGTCATCGCCTGCGACGTG GAGGCTGACTTTGCCGTCATTGCTGGTGTTTTCTAACTGGGGAGGCTATGCCCTGGCCTGCGCA CTCTACATCCTGTACTCATGTGCTGTCCACAGTCAGTACCTGAGGAAAGCAGTCGGACCCTCC AGGGCACCTGGAGTCAGGCCTGGACTCAGGCCCTCCCGTCGGTCATŢAAGGAAGAAAAAATG CTGGGCATCTTGGTGCAGCACAAAGTCCGGAGTGGCGTCTCGGGCATCGTGGGCATGGAGGTG GATGGGCTGCCCTTCCACAACACCCCACGCCGAGATGATCCAGAAGCTGGTGGACGTCACCACG ${\tt GCACAGGTG}$ ${\tt TAA}$ ${\tt CCGTCCATGTTCCGTGTGAGCAGAGTCCCTACCAACGGGCAGGTCTGCATC}$ CGGGGAGAATGCAGCTGCTTCTGGCGACAATCCTGCTAGTAAACACTGGTCTTCGGTGAGCAA GTGGACAAAGGACACATTTCTCTGGGGCTTTTTTAACTTTTATTCCTAAGACTCTAAAGGCGT TGATTTCAACCCTCCTTCACTCTGGCTTCTTCAGGCAACCCACGTGGTCTCCTATGAGAATCT TCTCGACAGTTACTTATGGGGACACTTGTGAACAATTAACTGCCAGGGCAGAGCATGAGAACA TTCTGTTACTCATGGTTTCAGTTACTCATAGCCAACTGCAGACCGAAAATACTAAATGAAAAA TTTCAGAAATAAACAACTCTTAAGTTTTAAAAAAAAA

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FIGURE 40

MPFTLHLRSRLPSAIRSLILQKKPNIRNTSSMAGELRPASLVVLPRSLAPAFERFCQVNTGPL PLLGQSEPEKWMLPPQGAISETRMGHPQFWKYEFGACTGSLASLEQYSEQLKDMVAFFLGCSF SLEEALEKAGLPRRDPAGHSQAGAYKTTVPCVTHAGFCCPLVVTMRPIPKDKLEGLVRACCSL GGEQGQPVHMGDPELLGIKELSKPAYGDAMVCPPGEVPVFWPSPLTSLGAVSSCETPLAFASI PGCTVMTDLKDAKAPPGCLTPERIPEVHHISQDPLHYSIASVSASQKIRELESMIGIDPGNRG IGHLLCKDELLKASLSLSHARSVLITTGFPTHFNHEPPEETDGPPGAVALVAFLQALEKEVAI IVDQRAWNLHQKIVEDAVEQGVLKTQIPILTYQGGSVEAAQAFLCKNGDPQTPRFDHLVAIER AGRAADGNYYNARKMNIKHLVDPIDDLFLAAKKIPGISSTGVGDGGNELGMGKVKEAVRRHIR HGDVIACDVEADFAVIAGVSNWGGYALACALYILYSCAVHSQYLRKAVGPSRAPGDQAWTQAL PSVIKEEKMLGILVQHKVRSGVSGIVGMEVDGLPFHNTHAEMIQKLVDVTTAQV

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 358-378, 517-539

N-glycosylation site.

amino acids 28-32

Tyrosine kinase phosphorylation site.

amino acids 444-452

N-myristoylation site.

amino acids 98-104, 102-108, 123-129, 149-155, 181-187, 190-196, 238-244, 308-314, 399-405, 413-419, 448-454, 477-483, 482-488, 487-493

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 233-244, 531-542

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FIGURE 41

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FIGURE 42

MQFHASVPSLMLFLPTGMPSPAPPALSAWQVHLSRSPQRPPPPGRQPLCPSPPGYLCTLSMLL LWHLSHCILLVYMFVSPSRL

Important features of the protein:

Signal peptide:

amino acids 1-22

Microbodies C-terminal targeting signal.

amino acids 81-83

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FIGURE 43

GTTTCCAACAAGGATGATATGAAGACTTCCCTGAAGAAAGTTGTGAAGGGACCTCCTACGAGA **TG**ATGATGCAGTGTGTCCCGCATGTTGGCCCACCCCCTGCATGTCATCTCAATGCGCTGCA TGGTCCAGTTTGTGGGACGGGAGGCCAAGTACAGTGGTGTGCTGAGCTCCATTGGGAAGATTT TCAAAGAGGAAGGGCTGCTGGGATTCTTCGTTGGATTAATCCCTCACCTCCTGGGCGATGTGG TTTTCTTGTGGGGCTGTAACCTGCTGGCCCACTTCATCAATGCCTACCTGGTGGATGACAGCT TCAGCCAGGCCTGGCCATCCGGAGCTATACCAAGTTCGTGATGGGGATTGCAGTGAGCATGC TGACCTACCCCTTCCTGCTAGTTGGCGACCTCATGGCTGTGAACAACTGCGGGCTGCAAGCTG GGCTCCCCCTTACTCCCCAGTGTTCAAATCCTGGATTCACTGCTGGAAGTACCTGAGTGTGC AGGGCCAGCTCTTCCGAGGCTCCAGCCTGCTTTTCCGCCGGGTGTCATCAGGATCATGCTTTG CCCTGGAGTAACCTGAATCATCTAAAAAACACGGTCTCAACCTGGCCACTGTGGGTGAGGCCT GCCGGGCTTCAGTTCCATATTTGCCATGTGTCTGTCCAGATGTGGGGTTGAGCGGGGGTGGGG CTGCACCCAGTGGATTGGGTCACCCGGCAGACCTAGGGAAGGTGAGGCGAGGTGGGGAGTTGG CAGAATCCCCATACCTCGCAGATTTGCTGAGTCTGTCTTGTGCAGAGGGCCAGAGAATGGCTT ATGGGGGCCCAGGTTGGATGGGGAAAGGCTAATGGGGTCAGACCCCACCCGTCTACCCCTCC AGTCAGCCCAGCGCCCATCCTGCAGCTCAGCTGGGAGCATCATTCTCCTGCTTTGTACATAGG GTGTGGTCCCCTGGCACGTGGCCACCATCATGTCTAGGCCTATGCTAGGAGGCAAATGGCCAG GCTCTGCCTGTGTTTTTCTCAACACTACTTTTCTGATATGAGGGCAGCACCTGCCTCTGAATG GGAAATCATGCAACTACTCAGAATGTGTCCTCCTCATCTAATGCTCATCTGTTTAATGGTGAT GCCTCGCGTACAGGATCTGGTTACCTGTGCAGTTGTGAATACCCAGAGGTTGGGCAGATCAGT GTCTCTAGTCCTACCCAGTTTTAAAGTTCATGGTAAGATTTGACCTCATCTCCCGCAAATAAA TGTATTGGTGATTTGGAAAAAAAAAAAAAAAAAA

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FIGURE 44

MMMQCVSRMLAHPLHVISMRCMVQFVGREAKYSGVLSSIGKIFKEEGLLGFFVGLIPHLLGDV VFLWGCNLLAHFINAYLVDDSFSQALAIRSYTKFVMGIAVSMLTYPFLLVGDLMAVNNCGLQA GLPPYSPVFKSWIHCWKYLSVQGQLFRGSSLLFRRVSSGSCFALE

Important features of the protein:

Signal peptide:

amino acids 1-18

Transmembrane domains:

amino acids 51-72, 97-114

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 160-163

N-myristoylation sites.

amino acids 34-39, 100-105, 123-128, 165-170

FIGURE 45

GAACCCACCAGAAGGAAGAACTCCAAACACCATCCGAACATCAGAAGGAGCAAACTCGTGACA CGCCACCTTTAAGAACCGTGACACTCAACGCTAGGGTCCGCGGCTTCATTCTTGAAGTCAGTG AGACCAAGAACCCACCAATTCCGGACACGGCAAAGTAACATCCTAGACATGGCTTTAGAGATC CACATGTCAGACCCCATGTGCCTCATCGAGAACTTTAATGAGCAGCTGAAGGTTAATCAGGAA GCTTTGGAGATCCTGTCTGCCATTACGCAACCTGTAGTTGTGGTAGCGATTGTGGGCCTCTAT CGCACTGGCAAATCCTACCTGATGAACAAGCTGGCTGGGAAGAACAAGGGCTTCTCTGTTGCA TCTACGGTGCAGTCTCACACCAAGGGAATTTGGATATGGTGTGTGCCTCATCCCAACTGGCCA AATCACACATTAGTTCTGCTTGACACCGAGGGCCTGGGAGATGTAGAGAAGGCTGACAACAAG AATGATATCCAGATCTTTGCACTGGCACTCTTACTGAGCAGCACCTTTGTGTACAATACTGTG AACAAAATTGATCAGGGTGCTATCGACCTACTGCACAATGTGACAGAACTGACAGATCTGCTC AAGGCAAGAAACTCACCTGACCTTGACAGGGTTGAAGATCCTGCTGACTCTGCGAGCTTCTTC CCAGACTTAGTGTGGACTCTGAGAGATTTCTGCTTAGGCCTGGAAATAGATGGGCAACTTGTC ACACCAGATGAATACCTGGAGAATTCCCTAAGGCCAAAGCAAGGTAGTGATCAAAGAGTTCAA AATTTCAATTTGCCCCGTCTGTGTATACAGAAGTTCTTTCCAAAAAAGAAATGCTTTATCTTT GACTTACCTGCTCACCAAAAAAAGCTTGCCCAACTTGAAACACTGCCTGATGATGAGCTAGAG CCTGAATTTGTGCAACAAGTGACAGAATTCTGTTCCTACATCTTTAGCCATTCTATGACCAAG ACTCTTCCAGGTGGCATCATGGTCAATGGATCTCGTCTAAAGAACCTGGTGCTGACCTATGTC AATGCCATCAGCAGTGGGGATCTGCCTTGCATAGAGAATGCAGTCCTGGCCTTGGCTCAGAGA GAGAACTCAGCTGCAGTGCAAAAGGCCATTGCCCACTATGACCAGCAAATGGGCCAGAAAGTG ACTCTACTAGATGCAAAACAGAATGACATTTGTAAACGGAACCTGGAAGCATCCTCGGATTAT TGCTCGGCTTTACTTAAGGATATTTTTTGGTCCTCTAGAAGAAGCAGTGAAGCAGGGAATTTAT TCTAAGCCAGGAGGCCATAATCTCTTCATTCAGAAAACAGAAGAACTGAAGGCAAAGTACTAT CGGGAGCCTCGGAAAGGAATACAGGCTGAAGAAGTTCTGCAGAAATATTTAAAGTCCAAGGAG GAGGCACAAGTGAAAGCAGAAGCTGAAAAGGCTGAAGCGCAAAGGTTGGCGGCGATTCAAAGG CAGAACGAGCAAATGATGCAGGAGAGGGGAGAGACTCCATCAGGAACAAGTGAGACAAATGGAG ATAGCCAAACAAATTGGCTGGCAGAGCAACAGAAAATGCAGGAACAACAGATGCAGGAACAG GCTGCACAGCTCAGCACATTCCAAGCTCAAAATAGAAGCCTTCTCAGTGAGCTCCAGCAC GCCCAGAGGGCTGTTAATAACGATGATCCATGTGTTTTACTC**TAA**AGTGCTAAATATGGGAGT TTCCTTTTTTTACTCTTTGTCACTGATGACACAACAGAAAAGAAACTGTAGACCTTGGGACAA TCAACATTTAAATAAACTTTATAATTATTAAA

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FIGURE 46

MALEIHMSDPMCLIENFNEQLKVNQEALEILSAITQPVVVVAIVGLYRTGKSYLMNKLAGKNK
GFSVASTVQSHTKGIWIWCVPHPNWPNHTLVLLDTEGLGDVEKADNKNDIQIFALALLLSSTF
VYNTVNKIDQGAIDLLHNVTELTDLLKARNSPDLDRVEDPADSASFFPDLVWTLRDFCLGLEI
DGQLVTPDEYLENSLRPKQGSDQRVQNFNLPRLCIQKFFPKKKCFIFDLPAHQKKLAQLETLP
DDELEPEFVQQVTEFCSYIFSHSMTKTLPGGIMVNGSRLKNLVLTYVNAISSGDLPCIENAVL
ALAQRENSAAVQKAIAHYDQQMGQKVQLPMETLQELLDLHRTSEREAIEVFMKNSFKDVDQSF
QKELETLLDAKQNDICKRNLEASSDYCSALLKDIFGPLEEAVKQGIYSKPGGHNLFIQKTEEL
KAKYYREPRKGIQAEEVLQKYLKSKESVSHAILQTDQALTETEKKKKEAQVKAEAEKAEAQRL
AAIQRQNEQMMQERERLHQEQVRQMEIAKQNWLAEQQKMQEQQMQEQAAQLSTTFQAQNRSLL
SELQHAQRAVNNDDPCVLL

Important features of the protein:

Transmembrane domains:

amino acids 31-49, 114-131

N-glycosylation sites.

amino acids 90-94, 144-148, 287-291, 563-567

N-myristoylation sites.

amino acids 45-51, 283-289

Prenyl group binding site.

amino acids 583-588

ATP/GTP-binding site motif A (P-loop).

amino acids 45-53

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FIGURE 47

CACTCATTCATTCCAAAGGGTCTCTCAAGGCAATGGTAATGTGCAAGGAGGTGATACCTAAAT TCTCTTGGTAGCCTTTAAATTCCTTGAAGCCCAGGACCATGTCTCACTTACCTTTGTGTTTCC ACTAACTAGTCTACCTCCTGGAATTGGCAGATACTCAGTGAAAGCCTGTGAAATAAGTGATGT CTATTTCTAGCATATTATTCTGAGATTTAATGATAGATTTAGTGATTGAATGAGATTTCCATT ATTAGGTCCTGAGTTAACTAATAATTACCTTTGAAATGTGTGGGGTTATTTGAGGCAATCAGGT GGTGACATTGAGCTCTCAGCCAGAGTTTGTTTCTGGAATTGATTCAGTTCCATTGCATTGATT TTTGTTCTCAGAAGCCAAGGTTTCCCATGAAAAATCATTCCCACTTGAATTGGGCTGTGATTC TTGCTGCGTTTAAGTAAAGGAAGCCTCTTGGTTCTAGTTCTGCAAACTTACACACTGAACTG GACAAGTTTTTGTTTAGAGTAATGGCTGGGAAAAGAGGAACCTTTCATTTTATTCAGAAGTCA AAAACAAAGGCCTCCCAGCCACCTGGAGATGTTTTGTTGCAGACACCAGCCTGGCTCTGTCTT TATGCCTAACAATTGAGCATCCAGTCTTCTTTGTGCTGGGACCATTGCTCAGCTCTGCAAGGG GAAAAGAGGGAGAAAGCCAGAGCTGCCAGGCTTCTTGCACTGGGGCCGGGGAGGGTTCCTGG GAAGCAGGTGCTCTCTGGCTTCTTGGTACGTGAGGCTCTCGGAGCTGCCTCTCCTCTGACCCT CAGGTCCTCACCGAGTTTGCTCCAGGAGTATATTGAAAACATACCCAGTGCTCTCTCAAGCAC CCACTGCTTAGAGGGCCCAGATTTCTTTTCCTTCTTTCCCTTGCAGAGCTGGAGACTGCATCG GGCATCTGGTGTTTAAACTAAACAGGAAAACTGACTAAAGGTCCACAGTGCTCATTGTGTAGA $\tt CTAGCTGCCCTCCG{\color{red} ATG} GGTGCTCTGATTATCAGTGGTTCCAGTGCAGGGCCTGTCACTAAAC$ AGGCCTCACTTCCTCCTTGGGGGGCTTTCCCATGGGAGGTGTGGCTTTTTACTCTACATGGAAA TGACTCTCTGCAGCCACAGAACACAGTCATTTTCTGAATTATCCCAGTCTCTCATGCGCCCTG GATTCCTCCAGATGCCTTATATCTCTTGTGCAAAGTTGTCTAAAATTTGGTTCCCAGCTTCCA AGCCTTGCCTTTTGGCCTTCCTGGAAGTATTTTTTGTTGATGAGTCGTCTGTCATTATTCTCTA **AA**CTTAGGGGATTACATGCCAATAAATCTATTGTTGAAAATGCACTAATACTATCGCAAAGAC GAAAATTCACAGGCTGAACCGTTGTAAGTCCATATGCTCCTCAACTTACATGTGTGATGGAGT TATGCCCAAATAAGTCCATCGTCAAGTTGAAAAATCAAAATCAAGCCATCTTAGGTTGAGGAC CATTTGTTTGTACCTCCAAAGATGTCATATCTTTAAACATACTCCCTAGCTTTTCTTTTTACT TTTTATTTTGAAGTAATTATAGAATCACAGAAAGTTGCAAAAAA

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FIGURE 48

MGALIISGSSAGPVTKQASLPPWGLSHGRCGFLLYMEMTLCSHRTQSFSELSQSLMRPGFLQM PYISCAKLSKIWFPASKPCLLAFLEVFLLMSRLSLFSKMICFLFLSFLFPPHIYTHAS

Important features of the protein:

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 88-107

Casein kinase II phosphorylation site.

amino acids 47-50

N-myristoylation site.

amino acids 24-29

FIGURE 49

TGGCTGTTGCTATGACAACGTGGCCACTGCAGCCGGTCCTCTTGGGGAAGGCTGTGTGGGCCAGCCCAGCCATGC CTCTGTGGGCCAATGTAACCGCTTCTGGTATGGCGGCTGCCATGGCAATGCCAATAACTTTGCCTCGGAGCAAGA GTGCATGAGCAGCTGCCAGGGATCTCTCCATGGCCCCGTCGTCCCCAGCCTGGGGCTTCTGGAAGGAGCACCCA CACGGATGGTGGCGCAGCAGTCCTGCAGGCGAGCAGGAACCCAGCAGCACAGGACAGGGCCGCGGTGCAGAG CTTTGGAGAATGGCCATGGGGCCAGGACTTGGGTCCAGGGCCCCTGGACTGGGTGGAGATGCCGGATCACCAGC GCCACCCTTCCACAGCTCCTCCTACAGATCTCACTTCCCACCTCTCCAGGATTAGCTTGGCAGGTGTGGAGCCCT CCTGGCAGAAAGATGGCCAGCCCATCTCCTCTGACAGGCACAGGCTGCAGTTCGACGGATCCCTGATCATCCACC $\verb|CCCTGCAGGCAGGAGGACGCGGGCACCTACAGCTGTGGCAGCACCCGGCCAGGCCGCGACTCCCAGAAGATCCAAC| \\$ TCCGCATTATAGGGGGTGACATGGCCGTGCTGTCTGAGGCTGAGCCGAGCCGCTTCCCTCAGCCCAGGGACCCAG CTCAGGACTTTGGCCAAGCGGGGCTGCTGGGCCCCTGGGGGCCATCCCCTCTTCACACCCACAGCCTGCAAACA GGCTGCGTTTGGACCAGAACCAGCCCCGGGTGGTGGATGCCAGTCCAGGCCAGCGGATCCGGATGACCTGCCGTG AGCCTGATGGCTCCCTGGTCATTAGCCGAGTGGCTGTAGAAGATGGCGGCTTCTACACCTGTGTCGCTTTCAATG GGCAGGACCGAGACCAGCGATGGGTCCAGCTCAGAGTTCTGGGGGGAGCTGACAATCTCAGGACTGCCCCCTACTG GGAACGGGCTACCTGTGCAGGCTGATGGCCACCGTGTCCACCAGTCCCCAGATGGCACGCTGCTCATTTACAACT TGCGGGCCAGGGATGAGGGCTCCTACATGTGCAGTGCCTACCAGGGGAGCCAGGCAGTCAGCCGCAGCACCGAGG CCAACTGTGATTTGATCCTGCAGGCCCAGCTTTGTGGCAATGAGTATTACTCCAGCTTCTGCTGTGCCAGCTGTT ${\tt CACGTTTCCAGCCTCAGCCCATCTGGCAG} \underline{{\tt TAG}} {\tt GGATGAAGGCTAGTTCCAGCCCCAGTCCAAAATAGTT}$ TACATTAGCTCTTTCAAAAACCCACCCAGTGTTTAGCCTCAACGGCAGCCAGTTACCAGCTTCTCTGTAGCCT TCAGCAGTGTTTGCATCTCTGACATAACCACAGGCTGCTGTTTTCAAGAAGAGCAATCTGTTTGGATAAGAAAAA ACGGAGTTTCACTCTTGTTGCCCAGGCTGGAGGGCAATGGCGCGATCTCAGCTCACCTGCAACCTCCGTCTCCTGG $\tt GTTCTTGATTCTCCTGTGTCAGCCTTCTGAGTAGCTGGGATTACAGATGCCTATCACCATGCCTGGGTAATTTTT$ TTTTTTGAGACAGAGTTTCGCACTTCTTGCCCAGGCTGGAGTACAATGGTGCGATCTTGGCTCACTGCAACCTCC ACCTCCTGGGTTCAAGCGCTTCTCCAGCCTCAGCCTCCTGAGTAGCTGGGATTACAGGTATGTGCCACCATGCCT GGCTAATTTTGTATTTTTGGTGGAGACGGGGTTTCTCCATGTTGGTCAGACTGGTCTTGAACTCCCGACCTCAGG TAATCCGCCCGCCTCCCAAAATGCTGGGATTAGAGGTGTGAGCCACTGTGCCCAGCCCATCAATGTGTT TTAAAGCTAGCTGTCAGGGTTCCACTTAATTTAAAGCTGGGCAGGGAGATGTGTAATGATTTCAAAGTTAACACC $\tt TGTTTGTTTTCTAAAGGGCATGCCAAGTCCTGCTGTATCAGGGAAGTATTCTGTGCTAAAATCAGCGATGGTTCA$ ACCCTTGTTGGCAAAATGGAATAGATGTTAAGACCTCAAATAGGGATTTGGGATGAAACAGCTGCAGTTAGCACT GTTATCTGAGCATGAAAGAACTGGAAACGCTCCTTACGTCGAGATGTTGGACCTTGAAGCCCTCCTGAGGCCAAC ATGCAAATCTGGCTGTGACGGTTCATCTGACACCTGTGTAAAGCTGACCAGCCTGCTCTGTACAGTGACAATGAG TTAAAAACAGCATTAGCAGGATGAGGATAGCAATGGGGAAGGGTTGTGGGCAATGCAGTAACAGGGAAATGGCTT CAGAAATGGTTTGAGTTGGAAGACAACATTCTTCATCTCTCAGGACTTCTAATTCCTTGATGCTAAAAGAAGAGG CATGGATTCTATGAGCTTCCAAGTCCCTTTCCACTTTAACCTTCTACAAATCTTTCAGAGGACTGCCTAGTAGCA ${\tt AAGGTTATTCCTGGACACAGGAAAGACGGGCATTACAGGGACCAAAGCTCTGAAAGGTGACTTTTATTACCAACA}$ AAATGTGGGCTGGGGCAGAGGTCTTTTTTCATTTAATACTGGAAAAATATTGAAGAGCATCCATGTTCACTTATG GCTGGTTTTGCTATAGAAATTGGAAAATAAAGGCCACTTTTTTG

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FIGURE 50

MGPVVPSLGLLEGAPTRMVAAAVLQASRNPASTGQGPRCRESPGLLVVSGGKTNSLGQGRPPT
PRPLENGHGGRSLGPGPLDWVEMPDHQRHPSTAPPTDLTSHLSRISLAGVEPSLVQAALGQLV
RLSCSDDTAPESQAAWQKDGQPISSDRHRLQFDGSLIIHPLQAEDAGTYSCGSTRPGRDSQKI
QLRIIGGDMAVLSEAELSRFPQPRDPAQDFGQAGAAGPLGAIPSSHPQPANRLRLDQNQPRVV
DASPGQRIRMTCRAEGFPPPAIEWQRDGQPVSSPRHQLQPDGSLVISRVAVEDGGFYTCVAFN
GQDRDQRWVQLRVLGELTISGLPPTVTVPEGDTARLLCVVAGESVNIRWSRNGLPVQADGHRV
HQSPDGTLLIYNLRARDEGSYMCSAYQGSQAVSRSTEVKVVSPAPTAQPRDPGRDCVDQPELA
NCDLILQAQLCGNEYYSSFCCASCSRFQPHAQPIWQ

Important features of the protein:

Signal peptide:

amino acids 1-16

Tyrosine kinase phosphorylation site.

amino acids 392-400

N-myristoylation sites.

amino acids 9-15, 50-56, 112-118, 146-152, 173-179, 195-201, 220-226, 229-235, 280-286, 306-312, 336-342, 397-403

Myelin PO protein.

amino acids 153-182

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FIGURE 51

CAGGCAGAAGCGAACAAAGACCCAGCAAGAGAAGGCAGAGGCTAAGACCCATCCCGTATCTGC TCTCCTGAAATAATTCTGGAGTCATGCCTGAAATGCCAGAGGACATGGAGCAGGAGGAAGTTA ACATCCCTAATAGGAGGGTTCTGGTTACTGGTGCCACTGGGCTTCTTGGCAGAGCTGTACACA AAGAATTTCAGCAGAATAATTGGCATGCAGTTGGCTGTGGTTTCAGAAGAGCAAGACCAAAAT ATGTTATAGTACATTGTGCAGCAGAGAGAGACCAGATGTTGTAGAAAATCAGCCAGATGCTG CCTCTCAACTTAATGTGGATGCTTCTGGGAATTTAGCAAAGGAAGCAGCTGCTGTTGGAGCAT TTCTCATCTACATTAGCTCAGATTATGTATTTGATGGAACAAATCCACCTTACAGAGAGGAAG ACATACCAGCTCCCCTAAATTTGTATGGCAAAACAAATTAGATGGAGAAAAGGCTGTCCTGG AGAACAATCTAGGAGCTGCTGTTTTGAGGATTCCTATTCTGTATGGGGAAGTTGAAAAGCTCG AAGAAAGTGCTGTGACTGTTATGTTTGATAAAGTGCAGTTCAGCAACAAGTCAGCAAACATGG ATCACTGGCAGCAGAGGTTCCCCACACATGTCAAAGATGTGGCCACTGTGTGCCGGCAGCTAG CAGAGAAGAATGCTGGATCCATCAATTAAGGGAACCTTTCACTGGTCTGGCAATGAACAGA TGACTAAGTATGAAATGGCATGTGCAATTGCAGATGCCTTCAACCTCCCCAGCAGTCACTTAA GACCTATTACTGACAGCCCTGTCCTAGGAGCACAACGTCCGAGAAATGCTCAGCTTGACTGCT CCAAATTGGAGACCTTGGGCATTGGCCAACGAACACCATTTCGAATTGGAATCAAAGAATCAC TTTGGCCTTTCCTCATTGACAAGAGATGGAGACAAACGGTCTTTCAT**TAG**TTTATTTGTGTTG GGTTCTTTTTTTTTAAATGAAAAGTATAGTATGTGGCACTTTTTAAAGAACAAAGGAAATA GTTTTGTATGAGTACTTTAATTGTGACTCTTAGGATCTTTCAGGTAAATGATGCTCTTGCACT AGTGAAATTGTCTAAAGAAACTAAAGGGCAGTCATGCCCTGTTTGCAGTAATTTTTCTTTTTA TCATTTTGTTTGTCCTGGCTAAACTTGGAGTTTGAGTATAGTAAATTATGATCCTTAAATATT TGAGAGTCAGGATGAAGCAGATCTGCTGTAGACTTTTCAGATGAAATTGTTCATTCTCGTAAC CTCCATATTTTCAGGATTTTTGAAGCTGTTGACCTTTTCATGTTGATTATTTTAAATTGTGTG AAATAGTATAAAAATCATTGGTGTTCATTATTTGCTTTGCCTGAGCTCAGATCAAAATGTTTG AAGAAAGGAACTTTATTTTTGCAAGTTACGTACAGTTTTTATGCTTGAGATATTTCAACATGT TATGTATATTGGAACTTCTACAGCTTGATGCCTCCTGCTTTTATAGCAGTTTATGGGGAGCAC TTGAAAGAGCGTGTGTACATGTATTTTTTTTTTCTAGGCAAACATTGAATGCAAACGTGTATTTT TTTAATATAAATATAAACTGTCCTTTTCATCCCATGTTGCCGCTAAGTGATATTTCATATGT GTGGTTATACTCATAATAATGGGCCTTGTAAGTCTTTTCACCATTCATGAATAATAATAATA TGTACTGCTGGCATGTAATGCTTAGTTTTCTTGTATTTACTTCTTTTTTTAAATGTAAGGACC ACATGTGATACATACAAAAGAATATAGTTTAATATGTATTGAAATAAAACACAATAAAATT

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FIGURE 52

MPEMPEDMEQEEVNIPNRRVLVTGATGLLGRAVHKEFQQNNWHAVGCGFRRARPKFEQVNLLD SNAVHHIIHDFQPHVIVHCAAERRPDVVENQPDAASQLNVDASGNLAKEAAAVGAFLIYISSD YVFDGTNPPYREEDIPAPLNLYGKTKLDGEKAVLENNLGAAVLRIPILYGEVEKLEESAVTVM FDKVQFSNKSANMDHWQQRFPTHVKDVATVCRQLAEKRMLDPSIKGTFHWSGNEQMTKYEMAC AIADAFNLPSSHLRPITDSPVLGAQRPRNAQLDCSKLETLGIGQRTPFRIGIKESLWPFLIDK RWRQTVFH

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 105-127

N-glycosylation site.

amino acids 197-201

N-myristoylation site.

amino acids 303-309

Short-chain dehydrogenases/reductases family proteins.

amino acids 18-30

FIGURE 53

TGGGCTCCCTCCAGCACTGCTGTTGCCTGCCTAAGATGGGTGACACTTGGGCCCAGCTTCCCTGGCCTGGGC CACCCCACCCAGCATGCTGCTGATCTCCCTCTCTTGGCAGCCGGGTTGATGCACTCGGATGCCGGCACCAGCT TGCCAATGGACACCCGAAACCTCAGCCTGGCCCACAACCGCATCACAGCAGTGCCGCCTGGCTACCTCACATGCT ACATGGAGCTCCAGGTGCTGGATTTGCACAACAACTCCTTAATGGAGCTGCCCCGGGGCCTCTTCCTCCATGCCA AGCGCTTGGCACACTTGGACCTGAGCTACAACAATTTCAGCCATGTGCCAGCCGACATGTTCCAGGAGGCCCATG GGCTAGTCCACATCGACCTGAGCCACAACCCTGGCTGCGGAGGGTGCATCCCCAGGCCTTTCAGGGCCTCATGC TGGTGACCCTGCAGATCGGTGGCAATCCCTGGGTGTGTGGCTGCACCATGGAACCCCTGCTGAAGTGGCTGCGAA TCTTCTCACTCACTGAGGAGGAGCTTCAAGGCCTGCCACCTGACCCTGACCCTGGATGATTACCTATTCATTGCGT TCGTGGGCTTCGTGGTCTCCATTGCTTCTGTGGCCACCAACTTCCTCCTGGGCATCACTGCCAACTGCTGCCACC GCTGCTGGCCACCAGACGCCCTCCCTGATTGCTCACTCTGGTTCCATGGTGACCTGGCTGCCTCAGTCATGGTTC AAGCAAGGTGGGGACACTCATTTTGTATGAGCATCTGCTTTTGGGCCAGGCGCACGCTAGGAATTGGGAACATCA AAGACTATATGTCAGGACTCTGAGCACGTCATTATGGAGGCCCAGAGGAGGAGCCATCATCTGTATCTAGCAATG TCCATGAGAATTATAAGATTAGAGTGATTTGTGAACTGGGTCATCAGGAAATATCTACTTTGTCAGGTAGGCAAA ACTTACTTGTATAGAGGGGGTGTGGCACAGAACTCAAACCTACCCCTCACCTCGACACCCAAAACTGTCAGCTC TCAGCAATGCCAGCCACTGCCTACAGGGAGTAAGAACACCTCTATGACAGCCCCTGGCCTCCTTCCACCAGCAGC TACCAGGTGAGACCACCTCCCAGTGACTGCCCCCATATGACCAAATGTCACCAGTTGGTGAGGTCCCAGGCAGCA GGCCCAGCAACTGGGGCAGCAAGAGTCCTGGCACCTTGGGATCCTAATCATGTGACTGTTCTTGCCACAGTGCTC ATGCCACAGGGTCTCACCAGGAAAGTGCACTGTGGGCCACAGACCCACAGCCTGGCAGCACCCAGAGCTAAAAGG GGACAAAGGCACAGTTATGACCATATGAGGCTTTGCATTTTCTTCTAAGCAACTTACCCACGTTAAGCATGA GGGTGAGAGAGCTATTAAATACTAAGCCCTTGCCAGTGTCAGGTACTTTGAAAAGCTCTCTGCACAAACCATTCC CTTTGACACACACACACACAATCTTTTGAGGTGAACGCTGTTGTTCCCATTTTACGGATGAGGCAACTAAGGCT CAGAGAGGTTAAAGTCACATGCCACTATGAGCAAGATAAAGTCTGTGCTCTTTCTACTGCCCCATCCAAGTTGGG GAACATCACCATTCCCTCTAGAGTTATATAAATTCAAATTCAACTAGAGCTGACAAAGTTCCTCATAAGGTCCAG GCACTCCTCTGGGCACTTTTATATCTATTGACTCACTTCTTTCAATTCTCACAGCAACACTGCCTGGTGGTTTTT ATTATCCCCATTTGACAGATGAATTAATCGTAGAGAGTTGAGTGACTTACCCAAGGTTGTCTGGATAAGCCCTAG AAGGAAGGCGGTAGGCAGCTCCATTCAGGGAAACTGCATCTAATCAGTCAAAAAATCAAGTAACTTTACGAG CAAAGCACAATTATCATCATCGTGGTCTTCTTCATCAGCTTTCGTCAGCAGCATCATTATCTTCCCTCTATTTGTT CAGCACCGGATAGTTCATGAGTATTTTTGCATCATTCTCCTTGACTTTTCACATCCCTGTGCAGGAGGTAAATCA AACATCAGTAATCCTGTTTTACAGATGGGGAAAAAAGTCTCAAGGTTGGATATGACTTGCTATGTGGCAAGGTTG GGGCTCAACCCTAACACAGTTCTCTTTCCAGTGCTTTCTCAAGTGCTTGGGGAAGAGAATGCCTCAGAAGGCTGG GTAGTGGGGCCCTGGAATTCAGCATCCATGAATGTGCTAGTGGATAAGCTAAATAGAAGGCAGCCAAACCCATCT GCTGTACAGATTGAACTATGCTCACGGTAGGGCAAATTGCAGGCTCTGAAACAGAGACTACACAGGTAACACCTG AATAGGAGACTCCTGCTTTACAATGTGTAGATAAAACATCAGCAATGGTGGCCATGGTGGCAGTCATGTGAAAAG TAAGATCTTTGGGAATCAAGAAAGGAAGCTGTGTTAACCACTCCTGCTCAAGCCCTGCTGCTGTTGCAAGAG ATACTAAGAGAGCAAGAAGCTATAGGTGAGAACCTCTGCAGTTTAGGAGAAGAACATCAAGGCACAGTCCAACA TGCTGATAAGTCTGGCCAGGAGGAGAATTAAAACAGGGGCTTTCCACACCTCCCTTGCCCCAAGCTCCAGCGGTA TTCTATCAGCCCATCCTCCTGGAAAGCCTGAAAGGAATGAAGGAGGCTAATAAGTCATCTTCCAGGAAGGCATCC CTCACTCGTGCTTCCCTGAGCTAGTCAACCAAAAGAGTCTTCAGAAACTTTGCTAGACCTGAAGTACTTGAACCT GTGTCCCCTGAATCTTTCTTACAACATCTGGGACAAATCCCTGGTCCTGTGACATCCGAAGCAGAACTGTGCCCT GCTCTCTCTCTGTGATGACCAAGGATGGTGAACTCAAGTTGTTCTCTACAAGCCAGGCCAGCAACCTAAATAC TTGGAGAGGAACTTTTAGAAACTATAATCCTGACAAAATAGAAAAGTTTCCCATAGGGGCATACCATAATACTAT ${\tt AATAACCTCCCAGGAACTATTGTTTGCCAAAATGTAGTTAATATTTTTAAGATATATGCTTTTTTGCATAGGAC}$ TAGAACCAGAAAAGACACCAAATGCCCCCTTGACATCAATGTCCTTTCTAGTGGGACAATTTGGTCTCCATTAAT ${\tt GCCAAACCTTTCTGAACAGGATACATGGCTTTTAAAGGACAGATGTTTCTCCTGCTGCTAGAAGTTCCTCAGTTT}$ ACTAGAGCACAATGAGGAAAGTATTCAACCTCCCTACTGCCAAGGAATTCCCTGCTTCTCCCCCACCGCCATCAT CTTGTCCAAGCTATCAGAAGCAACCTTCTAGAGATAATCTAACAATCCTGATTAGAATTGCTCCCATATCCCTGG GTCTGCGAGGTTCCTTGTATATTGGCTGTCCGCTGACTTGGGACAGATCTCTCTAGAACTTGGGTTCAGTTCTCT TGGTGCAAAAGTAATTGCGGTTTTTGCCATTAAAAATGATGGCAAAAATCCCCAATTACTTTTGCGTCAATCTAAT ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

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FIGURE 54

MLLISLLLAAGLMHSDAGTSCPVLCTCRNQVVDCSSQRLFSVPPDLPMDTRNLSLAHNRITAV PPGYLTCYMELQVLDLHNNSLMELPRGLFLHAKRLAHLDLSYNNFSHVPADMFQEAHGLVHID LSHNPWLRRVHPQAFQGLMQLRDLDLSYGGLAFLSLEALEGLPGLVTLQIGGNPWVCGCTMEP LLKWLRNRIQRCTADSQLAECRGPPEVEGAPLFSLTEESFKACHLTLTLDDYLFIAFVGFVVS IASVATNFLLGITANCCHRWSKASEEEEI

Important features of the protein:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 241-260

N-glycosylation sites.

amino acids 52-55, 81-84, 107-110

Tyrosine kinase phosphorylation site.

amino acids 148-154

N-myristoylation sites.

amino acids 11-15, 263-268

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 175-185

Leucine zipper pattern.

amino acids 77-98

FIGURE 55

GGCTGCGCCCAGGCCGGGCCCAGCAGCTGCGAACCGCCGCGCACCACCTGTTTCCGCGC TGTGCCGCGCTCTGGGCACAGCCTTGGAAAGTCAGGACCGCGACGCAGCAGAGCAGAAACCT TACAGAAACATGAAGCCCTCAACCATCTGCTACTCAGTTATTCGGGGCTGACGGCGGCTTCTA GAACATCCAGGTGTTCTGCAGATGCGAGAACTCATCCTGTAGTCACCAGATGGAGTCCCAAAC AGCCAAGCAGATGTAAGGCCTGTGCTGTGGCTCTGAGGCCCTGAATACAGAAGGGTCACTTTC TTAGTGGCCAAAGAGCAGTTGTTGACATTGATGTCTAATTATTGAACACGACCAGTCATTTTA CTGAGCTGCAGTGAGGAAACACTGACCATAGAAGATCAAGCCAAATGAGGGATTGCAAATTTC CTGATTCTTTTGAATTAGGATTCCAGATGGGGGCCTCATTTCTACAGCCCCCAACATTCCTAT AGCCGTTATCACTGCCATCACCACTGCCACCAGCATCTTCTTGCAGATTTCCACCCCTGCTCCC CAGAGACTTCCTGCTTTGAAAGTGAGCAGAAAGGAAGCTCTCAGAAAAATCTCTAGTGGTGGC TTTGTTGGCGGGAGTGAGTTTCTCAGGATTTCTTTATCCTCTTGTGGATTTTTTGCATCAGTGG GAAAACAAGAGGACAGAAGCCAAACTTTGTGATTATTTTGGCCGATGACATGGGGTGGGGTGA CCTGGGAGCAAACTGGGCAGAAACAAAGGACACTGCCAACCTTGATAAGATGGCTTCGGAGGG AATGAGGTTTGTGGATTTCCATGCAGCTGCCTCCACCTGCTCACCCTCCCGGGCTTCCTTGCT CACCGGCCGGCTTGGCCTTCGCAATGGAGTCACACGCAACTTTGCAGTCACTTCTGTGGGAGG CCTTCCGCTCAACGAGACCACCTTGGCAGAGGTGCTGCAGCAGGCGGGTTACGTCACTGGGAT AATAGGCAAATGGCATCTTGGACACCACGGCTCTTATCACCCCAACTTCCGTGGTTTTGATTA CTACTTTGGAATCCCATATAGCCATGATATGGGCTGTACTGATACTCCAGGCTACAACCACCC TCCTTGTCCAGCGTGTCCACAGGGTGATGGACCATCAAGGAACCTTCAAAGAGACTGTTACAC TGACGTGGCCCTCCTTTTATGAAAACCTCAACATTGTGGAGCAGCCGGTGAACTTGAGCAG CCTTGCCCAGAAGTATGCTGAGAAAGCAACCCAGTTCATCCAGCGTGCAAGCACCAGCGGGAG GCCCTTCCTGCTCTATGTGGCTCTGGCCCACATGCACGTGCCCTTACCTGTGACTCAGCTACC AGCAGCGCCACGGGCAGAAGCCTGTATGGTGCAGGGCTCTGGGAGATGGACAGTCTGGTGGG CCAGATCAAGGACAAAGTTGACCACACAGTGAAGGAAAACACATTCCTCTGGTTTACAGGAGA CAATGGCCCGTGGGCTCAGAAGTGTGAGCTAGCGGGCAGTGTGGGTCCCTTCACTGGATTTTG GCAAACTCGTCAAGGGGGAAGTCCAGCCAAGCAGACGACCTGGGAAGGAGGGCACCGGGTCCC AGCACTGGCTTACTGGCCTGGCAGAGTTCCAGTTAATGTCACCAGCACTGCCTTGTTAAGCGT GCTGGACATTTTCCAACTGTGGTAGCCCTGGCCCAGGCCAGCTTACCTCAAGGACGGCGCTT TGATGGTGTGGACGTCTCCGAGGTGCTCTTTGGCCGGTCACAGCCTGGGCACAGGGTGCTGTT CCACCCAACAGCGGGCAGCTGGAGAGTTTGGAGCCCTGCAGACTGTCCGCCTGGAGCGTTA CAAGGCCTTCTACATTACCGGTGGAGCCAGGGCGTGTGATGGGAGCATGGTGCCTGAGCTGCA GCATAAGTTTCCTCTGATTTTCAACCTGGAAGACGATACCGCAGAAGCTGTGCCCCTAGAAAG AGGTGGTGCGGAGTACCAGGCTGTGCTGCCCGAGGTCAGAAAGGTTCTTGCAGACGTCCTCCA AGACATTGCCAACGACAACATCTCCAGCGCAGATTACACTCAGGACCCTTCAGTAACTCCCTG CTGTAATCCCTACCAAATTGCCTGCCGCTGTCAAGCCGCA**TAA**CAGACCAATTTTTATTCCAC GAGGAGGAGTACCTGGAAATTAGGCAAGTTTGCTTCCAAATTTCATTTTTACCCTCTTTACAA ACACACGCTTTAGTTTTAGTCTTGGAGTTTAGTTTTGGAGTTAGCCTTGCATATCCCTTCTGTA TCCTGTCCCCCTCCACGCCGACCCGAGAGCAGCTGAGCTGCGCTGGGCTCTGGGCAGGGAGTG TGCCTTAATGGGAAGCACACGGGCTTTGGAGTCAGGCACAGGTGCCAGCTCCAGCTTTTGAAC AATGCCTGGCAACTTTAAAAAAAAAAAA

FIGURE 56

MGWLFLKVLLAGVSFSGFLYPLVDFCISGKTRGQKPNFVIILADDMGWGDLGANWAETKDTAN LDKMASEGMRFVDFHAAASTCSPSRASLLTGRLGLRNGVTRNFAVTSVGGLPLNETTLAEVLQ QAGYVTGIIGKWHLGHHGSYHPNFRGFDYYFGIPYSHDMGCTDTPGYNHPPCPACPQGDGPSR NLQRDCYTDVALPLYENLNIVEQPVNLSSLAQKYAEKATQFIQRASTSGRPFLLYVALAHMHV PLPVTQLPAAPRGRSLYGAGLWEMDSLVGQIKDKVDHTVKENTFLWFTGDNGPWAQKCELAGS VGPFTGFWQTRQGGSPAKQTTWEGGHRVPALAYWPGRVPVNVTSTALLSVLDIFPTVVALAQA SLPQGRRFDGVDVSEVLFGRSQPGHRVLFHPNSGAAGEFGALQTVRLERYKAFYITGGARACD GSMVPELQHKFPLIFNLEDDTAEAVPLERGGAEYQAVLPEVRKVLADVLQDIANDNISSADYT QDPSVTPCCNPYQIACRCQAA

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 353-373

N-glycosylation sites.

amino acids 117-120, 215-218, 356-359, 397-500

N-myristoylation sites.

amino acids 12-17, 33-38, 52-57, 97-102, 101-106, 113-118, 158-163, 328-333, 388-393, 418-423, 435-440, 436-441

Amidation site.

amino acids 382-385

Sulfatases signature 2.

amino acids 129-138

FIGURE 57

TGGACAAGACACCTCCAGGAGCCCAGCTCACAGCCACCGGTACCTTCTTCCAGGACAAGCTGG GGGCCTCCATGGGCGCCTGAGGGCCAGGCGCCAGGGCCGTGGGCACGAGT**ATG**GTGAGACACC AGCCCCTGCAGTACTACGAGCCACAGCTGTGCCTCTCCTGCCTCACGGGCATCTACGGCTGCC GTTGGAAGCGCTACCAGCGCTCCCATGATGATACCACACCGGGCACAGCGCCATTCCTGCATG TGGGGGCTGTGGCAGCAGTCACCATGCTCTCCTGGATCGTGGCAGGACAGTTCGCCCGTGCAG AGCGGACCTCCTCCCAGGTGACCATTCTCTGTACCTTCTTCACCGTGGTGTTTTGCCCTCTACC TGGCCCCTCTCACCATCTCCTCTCCCTGCATCATGGAGAAGAAGACCTCGGCCCCAAGCCTG CTCTCATTGGCCACCGCGGGGCCCCCATGCTGGCTCCAGAGCACACGCTCATGTCCTTCCGGA AGGCCCTCGAGCAGAAGCTGTACGGGCTCCAGGCTGACATTACCATCAGCCTGGACGGCGTGC CCTTCCTCATGCATGACACCACCTGCGGCGCCACCAACGTGGAGGAGGAGTTCCCGGAGC TGGCCCGCAGGCCTGCCTCCATGCTTAACTGGACCACCCTGCAGAGACTCAACGCTGGCCAGT CCCAGAACCAGTCCATCTGCAGCCTGGCAGAGCTCCTGGAGCTGGCCAAGGGCAATGCCACAC TGCTGCTCAACCTGCGTGACCCGCCCCGGGAGCACCCCTACCGCAGCAGTTTTATCAACGTGA CTCTGGAGGCCGTGCTGCACTCCGGCTTCCCCCAGCACCAGGTCATGTGGCTGCCTAGCAGGC AGAGGCCCCTGGTGCGGAAGGTGGCTCCCGGCTTCCAACAGACATCAGGCTCCAAGGAGGCAG TCGCCAGCCTGCGGAGAGGCCACATCCAGCGGCTGAACCTGCGCTACACTCAGGTGTCCCGCC AGGAGCTCAGGGACTACGCGTCCTGGAACCTGAGTGTGAACCTCTACACAGTCAACGCACCGT GGCTCTTCTCCCTGCTGTGGTGTGCGGGGGTCCCATCCGTCACCTCTGACAACTCCCACACCC TGTCCCAGGTGCCTTCCCCCCTCTGGATCATGCCCCCGGACGAGTACTGTCTCATGTGGGTCA CTGCCGACCTGGTCTCCTTCACCCTCATCGTGGGCATCTTCGTGCTCCAGAAGTGGCGCCTGG GTGGCATACGGAGCTACAACCCTGAGCAGATCATGCTGAGTGCTGCGGTGCGCCGGACCAGCC GGGACGTCAGCATCATGAAGGAGAAGCTTATTTTCTCAGAGATCAGCGATGGTGTAGAGGTCT CCGATGTGCTCTCCGTATGTTCAGACAACAGTTATGACACATATGCCAACAGCACCGCCACCC CTGTGGGCCCCGAGGGGGTGGCAGCCACACAAGACCCTCATAGAGCGGAGTGGGCGT<u>TAG</u>C TGAAGACATGTCTGTCCCACCTGTACCTGACACAGAAGCTGGGGAGCCTAGGAGAGCTGGTGG AAGTGTGTCTGAACTCGGAGTGCTCTGGGAGCGGGCTCCACAGCCTCCTTGTGGGCTCCAGGCC CCTTGTCAGCCGCAGCCTCTCTTGAGGGGGGACTCCCTGTCTCCTGAGGCCCAGCTGGGCCAGG ACTCCATCCTTTCAGATGCCCCTGCAGGCCTGGGGCTCCTTCTGGGAAGTATGGGGCCTAGGG CTTGGTCCCCTCTTCTGAGGCCCTCTCCTGTATCCCGACCTGGAAGCTTTGATGGGTCATGG GCCATGCCATACCCCCTGTGGCAATGGAGTGTGTGGATGCTCACCTGTGCCATCTGTCCTCCT GTCTGTGCCAGGAGGCACCTGAGTTCTCTGCTGTTATCCTGCCCCAAGGGCCTGGGCCGAGGCC TCTACCTGAAGCAACTCTGCTCTTCCTGTCAGTCTCAAAGCACAAGGAGGTTCAGCCCAGGAG GAAGCCAGCTGCAATGTGGAGACACGTCCTCCTCCCCAACCCACCTCATGCCACCGCCAACCC CCTGCCCAGGAGCGGCCTGAGCCACGTCCCCTAGGAGCAGCTGGAGATGGCCAAAAGAGTG AGCTCAGGACTACTGGATCCCATGCCCAGGTGTCCAGCAGACCTCAAGGCAGAAGGGTCACCT AACCCAGGAGTCCACAGACTGATGTGACCTCAGGTTCCCACATCAGTGGCCACAGGGCAGGGC AGGGAACCTAGGGCCCTTGGCCAATGTGATTAAAGCTGCCATCTTGAAA

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FIGURE 58

MVRHQPLQYYEPQLCLSCLTGIYGCRWKRYQRSHDDTTPGTAPFLHVGAVAAVTMLSWIVAGQ
FARAERTSSQVTILCTFFTVVFALYLAPLTISSPCIMEKKDLGPKPALIGHRGAPMLAPEHTL
MSFRKALEQKLYGLQADITISLDGVPFLMHDTTLRRTTNVEEEFPELARRPASMLNWTTLQRL
NAGQWFLKTDPFWTASSLSPSDHREAQNQSICSLAELLELAKGNATLLLNLRDPPREHPYRSS
FINVTLEAVLHSGFPQHQVMWLPSRQRPLVRKVAPGFQQTSGSKEAVASLRRGHIQRLNLRYT
QVSRQELRDYASWNLSVNLYTVNAPWLFSLLWCAGVPSVTSDNSHTLSQVPSPLWIMPPDEYC
LMWVTADLVSFTLIVGIFVLQKWRLGGIRSYNPEQIMLSAAVRRTSRDVSIMKEKLIFSEISD
GVEVSDVLSVCSDNSYDTYANSTATPVGPRGGGSHTKTLIERSGR

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domains:

amino acids 47-61, 77-93, 335-350, 380-399

N-glycosylation sites.

amino acids 182-186, 217-221, 233-237, 255-259, 329-333, 462-466

Tyrosine kinase phosphorylation site.

amino acids 130-139

N-myristoylation sites.

amino acids 21-27, 48-54, 294-300, 404-410, 442-448, 473-479

FIGURE 59

CCTGAGCAAACACAGCCGGAGTGTTCCCAAGGCCAAA**ATG**CTGAGAACGTCCACTCCTAA TCTGTGTGTGGTGTCTGCATTGCCGGGCCCCCTGGCTCTCTTCTGGCATTCTCTGCCTCTGCCT CATATTCTTGTTAGGCCAGGTGGGCTTGCTGCAGGGACACCCCCAGTGCCTGGATTACGGGCC CCCTTTCCAGCCCCTCTGCACCTTGAGTTTTGCTCTGACTATGAGTCCTTCGGCTGCTGTGA TCAGCACAAGGACCGCCGCATCGCTGCCCGGTACTGGGACATCATGGAATATTTTGATCTGAA GAGACATGAGCTGTGTGGAGATTACATTAAAGACATCCTTTGCCAGGAGTGCTCGCCCTACGC AGCCCACCTCTACGACGCCGAAAACACCCAGACGCCTCTCCGGAATCTCCCGGGCCTCTGCTC TGATTACTGCTCTGCCTTCCATTCTAACTGTCACTCAGCCATTTCCCTGCTGACCAATGACCG CGGCCTCCAGGAGTCTCATGGAAGGGACGGTACCCGCTTCTGCCACCTCCTGGACCTTCCTGA CAAGGACTATTGCTTCCCTAATGTCCTGAGGAACGACTATCTCAACCGCCACCTGGGCATGGT GGCCCAAGATCCTCAGGGCTGCCTGCAGCTCTGCCTGAGCGAGGTGGCCAACGGGCTGAGGAA CCCCGTCTCCATGGTCCATGCTGGGGACGGCACCCATCGCTTCTTTGTTGCCGAGCAGGTAGG AGTGGTGTGGGTCTACCTCCTGATGGGAGTCGCCTGGAGCAACCCTTCCTGGACCTCAAGAA CATCGTGTTGACCACCCCATGGATCGGGGATGAGAGAGGCTTCTTGGGGTTGGCTTTTCACCC CAAATTCCGCCACAATCGCAAGTTCTATATTTATTATTCGTGCCTGGACAAGAAGAAGGTAGA AAAGATCCGAATTAGTGAGATGAAGGTTTCTCGGGCTGATCCTAACAAAGCTGACCTGAAATC AGAGAGGGTCATCTTGGAGATTGAAGAACCAGCCTCAAACCATAATGGCGGACAACTTCTTTT TGGCCTGGATGGCTATATGTACATATTCACTGGGGACGGGGGACAGGCTGGAGATCCCTTTGG CCTGTTTGGAAATGCTCAGAACAAAGTTCCCTGCTGGGAAAAGTTTTAAGGATCGATGTGAA CAGGGCAGGCTCACATGGCAAGCGGTACCGAGTCCCCTCGGACAATCCATTTGTTTCTGAGCC AGGGGCCCACCCGCCATCTATGCCTATGGGATCAGGAACATGTGGCGTTGTGCTGTGGACCG AGGGGACCCCATCACGCGCCAGGGCCGAGGCCGGATATTCTGTGGGGACGTGGGCCAGAACAG TGCATGTTATGACAAAAACTTTGTCACAATGCCTCTTTGGATGATGTTCTGCCAATCTATGC TTATGGCCATGCAGTGGGGAAGTCAGTCACTGGAGGTTATGTCTATCGTGGTTGTGAATCCCC AAATCTCAATGGCCTGTATATCTTTGGAGACTTCATGAGTGGTCGACTTATGGCTTTGCAGGA AGATAGAAAAAACAAGAAATGGAAGAAGCAGGATCTTTGCCTGGGCAGCACCACGTCCTGTGC CTTCCCAGGGCTGATCAGCACCCATAGCAAGTTCATCATCTCCTTTGCTGAAGATGAAGCAGG GGAGCTGTATTTCCTGGCGACCTCTTACCCAAGTGCCTATGCACCACGTGGATCTATTTACAA GTTTGTTGACCCCTCAAGGCGAGCACCCCCAGGCAAGTGCAAATACAAGCCAGTGCCCGTGAG AACCAAGAGTAAGCGGATCCCGTTCAGACCACTCGCCAAGACAGTCTTGGACTTGCTAAAGGA ACAATCAGAGAAAGCTGCTAGAAAATCTTCCAGTGCAACCTTAGCTTCTGGCCCAGCCCAGGG TTTGTCTGAGAAAGGCTCCTCCAAGAAGCTGGCTTCTCCTACAAGCAGCAAGAATACATTGCG AGGGCCTGGTACAAAGAAGAAGCCAGAGTGGGGCCCCACGTCCGCCAGGGCAAGAGGAGAAA GAGCCTGAAAAGCCACAGTGGCAGGATGAGGCCATCAGCAGAGCAGAAGCGAGCTGGCAGAAG TCTCCCT<u>TGACCTATTGGTCAAGGTGGCCGACAGGGTGACGTGAGAGAGGAGAGCCACCTCAT</u> CAAATGAAAGTCACTGCTGAATAAAGACCTTAGAAGTCTGGGAAGCCAGGGTAGAGGTGGGGC GTATGCAGTGCTTCTGTGGGAGACCATATCCCAGATTGCTGGTGCACCTGGGTTATGGTAAGC ACTAGTCCATGAGCCTGCTTGGAATCACACTGGATGTCTCCGTTTTGTCTTGTAAATGCCTAC AACCTGAGGTAATAAATCAACATTTGCTCA

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FIGURE 60

MLRTSTPNLCGGLHCRAPWLSSGILCLCLIFLLGQVGLLQGHPQCLDYGPPFQPPLHLEFCSD
YESFGCCDQHKDRRIAARYWDIMEYFDLKRHELCGDYIKDILCQECSPYAAHLYDAENTQTPL
RNLPGLCSDYCSAFHSNCHSAISLLTNDRGLQESHGRDGTRFCHLLDLPDKDYCFPNVLRNDY
LNRHLGMVAQDPQGCLQLCLSEVANGLRNPVSMVHAGDGTHRFFVAEQVGVVWVYLPDGSRLE
QPFLDLKNIVLTTPWIGDERGFLGLAFHPKFRHNRKFYIYYSCLDKKKVEKIRISEMKVSRAD
PNKADLKSERVILEIEEPASNHNGGQLLFGLDGYMYIFTGDGGQAGDPFGLFGNAQNKSSLLG
KVLRIDVNRAGSHGKRYRVPSDNPFVSEPGAHPAIYAYGIRNMWRCAVDRGDPITRQGRGRIF
CGDVGQNRFEEVDLILKGGNYGWRAKEGFACYDKKLCHNASLDDVLPIYAYGHAVGKSVTGGY
VYRGCESPNLNGLYIFGDFMSGRLMALQEDRKNKKWKKQDLCLGSTTSCAFPGLISTHSKFII
SFAEDEAGELYFLATSYPSAYAPRGSIYKFVDPSRRAPPGKCKYKPVPVRTKSKRIPFRPLAK
TVLDLLKEQSEKAARKSSSATLASGPAQGLSEKGSSKKLASPTSSKNTLRGPGTKKKARVGPH
VRQGKRRKSLKSHSGRMRPSAEQKRAGRSLP

Important features of the protein:

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 17-36

N-glycosylation sites.

amino acids 372-376, 480-484

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 645-649, 699-703

Tyrosine kinase phosphorylation site.

amino acids 81-89

N-myristoylation sites.

amino acids 11-17, 37-43, 156-162, 165-171, 357-363, 365-371, 368-374, 408-414, 459-465, 548-554, 557-563

Amidation sites.

amino acids 391-395, 696-700

Cell attachment sequence.

amino acids 428-431

Leucine zipper pattern.

amino acids 25-47

FIGURE 61

CTCCATTAAACCACCACCAGCTCCCCAAGCCACCCCTTCAGCCATGAAGTTCCTGCTCCTGGT GAGTAACACCCCAGGATACTGCAGGACATGTTGCCACTGGGGGGAGACAGCATTGTTCATGTG CAACGCTTCCAGAAAATGCTGCATCAGCTACTCCTTCCTGCCGAAGCCTGACCTACCACAGCT GACCGTAACATCATAATAACCACTGCTATCGCCTCCACCAACTCAGAGAAATATCATTTCCAC AGTTCCAATTCCTCCTACATTGCTGAGTACTAGCCAAGGCTCCTCTTTATGGGGCAGATATCT TTTGTATCTATCTTACGAGAACAATCATCATGCAGATTCGTCCACAGGGGATCTGTCAGTTTG GGTCCTCCAAATGAAAAATGTCAAGACAGAATTGGACATGCAAAAGATTGACTGGGAGAACAC CTGGCCTGATACGTGTCAAAGGAGAGGGGATAGAGGAGGATTGAATAGAAGGAGACTAAGAC TGCAGCTCTAAGAAAGTCTCAGCCAAACAGATGGGGAGGCCCAAAGCAAGGCTTGCCCCTCAG AGGAGCTCACGCAGGCAGGAATAGCCAGGTTCTCATATCCCAGGGGTTCAGACTTGGCTGAG AACAGCCCCTGGAGAACATGGGGTGACTGCTACCATAGGTCTGGAAGTATGAGGCTGTCCACC AACTATCCCCTTGAAGCAAGTTCTCTTGAAAGGAAATCTAAACAGTGCACCCCCATGGCTGCC ACGGAGTATAAGGAGGAGAGAAAGGAGCTGAAAGTCTAGGTTTGGCCAGCTAGGTAGACTGA TAGTACACCCCAAAAGCAAGGATGGCATGATGCTGGTGACTCAAACGTGCCTACTCATGGTGT CAAATTGGCATAATCCTCTTGGGAAGCTGTGTGGAAATAAGCACAGAGAAGCAGAACTCTAAT TGCTTAATCCACTAAACATTACTTCTGGGAATTGGCTCATCATAAATTATCCAAGAGAAAGCA CAAAGTTATGGGCACAAAGGTTTTCCATATAATATTATTAAAAATGCTGAGAAAATGAAAAAA TAATGGAACATAATAACATTATTCAAAATTGCATTTATGCTATAGTTGTCAAAATTGTCTCCT CTTCTATCTGAGAAGAACAAACCAAAACACTCAGGCCTAAATAATTAAAAAACGGTCCTAAAAA CTAGCAAACCAGATAAGAAAAGATGTTAATGCCCATTCCCTAACTTATGTCTTAGACCAAAAT TAATTCTAGATGGTTTTAAAATGACAGTGTAAAAGTAAAGTATTAAAAGATTGTGTGGTCAAA TATTCAATTTAAGAGCAAGGAAATTCTTATAAATATAACAATAGAGGCAGAACTCATGTAAGA ATTCATCCATCTTATTGGGTATTGCAGGAGTTCATTCCTTTTTGTTTATAAATACTCTTCCGT CATATGAATAGTATTCATTTGTATACTGGTTTGTTGATGGACATTTGGGTTGTTCCCAGTTTA TGGCTATTACAAATAAAGCTTCTATGAACATTTATGTACA

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FIGURE 62

 ${\tt MKFLLLVLAALGFLTQVIPASAGGSKCVSNTPGYCRTCCHWGETALFMCNASRKCCISYSFLP} \\ {\tt KPDLPQLIGNHWQSRRRNTQRKDKKQQTTVTS}$

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 1-22

N-glycosylation site.

amino acids 50-53

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 79-82

N-myristoylation site.

amino acids 23-28

FIGURE 63

GCGGAGCGCCTGGGAGAGGAGGAGGCCGACCTGCCGAGATCGAGGCGACCGGCACCTGGGC GCTGCTGCTGCGCTGCTCCTGCTGCTGACGCTGCCGCTGTCCGGGACCAGGGCCCG AGGCCACCTGCCCCCGGGCCCACGCCGCTACCACTGCTGGGAAACCTCCTGCAGCTACGGCC CGGGGCGCTGTATTCAGGGCTCATGCGGCTGAGTAAGAAGTACGGACCGGTGTTCACCATCTA CCTGGGACCCTGGCGGCCTGTGGTGGTCCTGGTTGGGCAGGAGGCTGTGCGGGAGGCCCTGGG AGGTCAGGCTGAGGAGTTCAGCGGCCGGGGAACCGTAGCGATGCTGGAAGGGACTTTTGATGG CCATGGGGTTTTCTTCTCCAACGGGGAGCGGTGGAGGCAGCTGAGGAAGTTTACCATGCTTGC TCTGCGGGACCTGGGCATGGGGAAGCGAGAAGGCGAGGGCTGATCCAGGCGGAGGCCCGGTG GGCCACCTCCAACGTAGTCTGCTCCCTCCTCTTTGGCCTCCGCTTCTCCTATGAGGATAAGGA GTTCCAGGCCGTGGTCCGGGCAGCTGGTGGTACCCTGCTGGGAGTCAGCTCCCAGGGGGGTCA GACCTACGAGATGTTCTCCTGGTTCCTGCGGCCCCTGCCAGGCCCCCACAAGCAGCTCCTCCA CCACGTCAGCACCTTGGCTGCCTTCACAGTCCGGCAGGTGCAGCAGCACCAGGGGAACCTGGA TGCTTCGGGCCCCGCACGTGACCTTGTCGATGCCTTCCTGCTGAAGATGGCACAGGAGGAACA TGGGACGATGACGGTCAGCACCACGGTCGGCTATACCCTCCTGCTCCTGATGAAATACCCTCA TGTCCAAAAGTGGGTACGTGAGGAGCTGAATCGGGAGCTGGGGGGCTGGCCAGGCACCAAGCCT AGGGGACCGTACCCGCCTCCCTTACACCGACGCGGTTCTGCATGAGGCGCAGCGGCTGCTGGC GCTGGTGCCCATGGGAATACCCCGCACCCTCATGCGGACCACCCGCTTCCGAGGGTACACCCT GCCCCAGGGCACGGAGGTCTTCCCCCTCCTTGGCTCCATCCTGCATGACCCCAACATCTTCAA GCACCCAGAAGAGTTCAACCCAGACCGTTTCCTGGATGCAGATGGACGGTTCAGGAAGCATGA GGCGTTCCTGCCCTTCTCCTTAGGGAAGCGTGTCTGCCTTGGAGAGGGCCTGGCAAAAGCGGA GCTCTTCCTCTTCACCACCATCCTACAAGCCTTCTCCCTGGAGAGCCCGTGCCCGCCGGA CACCCTGAGCCTCAAGCCCACCGTCAGTGGCCTTTTCAACATTCCCCCAGCCTTCCAGCTGCA AGTCCGTCCCACTGACCTTCACTCCACCACGCAGACCAGA**TGA**AGGAAGGCAACTTGGAAGTG GTGGGTGCCCAGGACGGTGCCTCCAGCCTCAACAGTGGGCATGGACAGGGTTAATGTCTCCAG AGTGTACACTGCAGGCAGCCACATTTACACGCCTGCAGTTGTTTTCCGGAGTCTGTCCCACGG CCCACACGCTCACTTGACTCATGCTGCTAAGATGCACAACCGCACACCCATACAACTACAA GGGCCACAAAGCAACTGCTGGGTTAGCTTTCCACAGACATAAATATAGTCCATCTGCAATCAC AAGCACATAGCCAGGTAACCCACCAACTCCCCTGGATCTGCAGCCCACACGTGGGAGTCTGGC TGTCACCTTCACAAGCCACAGAAACGGCCACACATGTTCACAGCTCACACGCCCTCTCCATTC ATCGAACTTCTCAGTGTCCCTGTCCCTGGTGCCTGGCACAGGGAACAGCATGCCCCCTCCGGG GTCATGCCACCCAGAGACTGTCGCTGTCTATGGCCCCAACTCATGCTCCCTCTCTTGGCTACA CCACTCTCCCAGCCTGTGACCACCGATGTCCACACCCCCCAACCACTTGTCCACACAGCTAC CCACGTACAACATCGTCCTGGCTCCCCAGAGTATCTTCCCACTGAGACACGCCGCCCCCACAG AGGCACAGTCCCCAGCCACCTCTGCAACTGCAGCCCTCAGTCACCCCTTTTTAAGCACCCTGA TTCTACCAAATGCAAACACATCTGGGTCTGCGATTATGCACAGAGACTTTGGACATACGAGGA CCCTCAGACCGGAGGAACACCTGCCCAACCCCAACACGTGCTTATGTAACCACGTGGAAAGCG GCCCCTGCTGCCCCCCACACACACACACACCCCACTGATCTACAGCCCCTGTTCGGCGTCA GAGTCCCCACTAGACCCAGTGGAAGGGGTTAGAGACCAAGTAGGGGCCAGTTTCCAATTCACC CTGTCAGGGAGTGAGCCGGATCTGACGTTCCTTGTGACTTAAGGGTCCGGCTTGGGAATTAAA

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FIGURE 64

MEATGTWALLLALALLLLTLALSGTRARGHLPPGPTPLPLLGNLLQLRPGALYSGLMRLSKK YGPVFTIYLGPWRPVVVLVGQEAVREALGGQAEEFSGRGTVAMLEGTFDGHGVFFSNGERWRQ LRKFTMLALRDLGMGKREGEELIQAEARCLVETFQGTEGRPFDPSLLLAQATSNVVCSLLFGL RFSYEDKEFQAVVRAAGGTLLGVSSQGGQTYEMFSWFLRPLPGPHKQLLHHVSTLAAFTVRQV QQHQGNLDASGPARDLVDAFLLKMAQEEQNPGTEFTNKNMLMTVIYLLFAGTMTVSTTVGYTL LLMKYPHVQKWVREELNRELGAGQAPSLGDRTRLPYTDAVLHEAQRLLALVPMGIPRTLMRT TRFRGYTLPQGTEVFPLLGSILHDPNIFKHPEEFNPDRFLDADGRFRKHEAFLPFSLGKRVCL GEGLAKAELFLFFTTILQAFSLESPCPPDTLSLKPTVSGLFNIPPAFQLQVRPTDLHSTTQTR

Important features of the protein:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 294-313

Glycosaminoglycan attachment site.

amino acids 99-103

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 128-132

N-myristoylation sites.

amino acids 51-57, 109-115, 115-121, 188-194, 207-213, 257-263, 284-290, 339-345, 370-376, 444-450

Amidation sites.

amino acids 140-144, 435-439

Leucine zipper pattern.

amino acids 32-54, 39-61

Cytochrome P450 cysteine heme-iron ligand signature.

amino acids 433-443

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FIGURE 65

 $\tt CGGACGCGTGGGGCCGT{\color{red} {\bf ATG}} CGCGGCTCTGTGGAGTGCACCTGGGGTTGGGGGCACTGTGCCCC{\color{red} {\bf CGGACGCGTGGGGGCACTGTGCCCC} }$ CCAGCCCCTGCTCCTTTGGACTCTACTTCTGTTTGCAGCCCCATTTGGCCTGCTGGGGGAGA ATATACGGGCAGTGGGCACCAATTCCACACTGCACTATGTGTGGAGCAGCCTGGGGCCTCTGG CAGTGGTAATGGTGGCCACCAACACCCCCCACAGCACCCTGAGCATCAACTGGAGCCTCCTGC TATCCCCTGAGCCCGATGGGGGCCTGATGGTGCTCCCTAAGGACAGCATTCAGTTTTCTTCTG CCCTTGTTTTTACCAGGCTGCTTGAGTTTGACAGCACCAACGTGTCCGATACGGCAGCAAAGC CTTTGGGAAGACCATATCCTCCATACTCCTTGGCCGATTTCTCTTGGAACAACATCACTGATT CATTGGATCCTGCCACCCTGAGTGCCACATTTCAAGGCCACCCCATGAACGACCCTACCAGGA CTTTTGCCAATGGCAGCCTGGCCTTCAGGGTCCAGGCCTTTTCCAGGTCCAGCCGACCAGCCC AACCCCTCGCCTCCTGCACACAGCAGACACCTGTCAGCTAGAGGTGGCCCTGATTGGAGCCT CTCCCCGGGGAAACCGTTCCCTGTTTGGGCTGGAGGTAGCCACATTGGGCCAGGGCCCTGACT GCCCTCAATGCAGGAGCAGCACTCCATCGACGATGAATATGCACCGGCCGTCTTCCAGTTGG ACCAGCTACTGTGGGGCTCCCTCCCATCAGGCTTTGCACAGTGGCGACCAGTGGCTTACTCCC AGAAGCCGGGGGGCCGAGAATCAGCCCTGCCCTGCCAAGCTTCCCCTCTTCATCCTGCCTTAG CATACTCTCTCCCCAGTCACCCATTGTCCGAGCCTTCTTTGGGTCCCAGAATAACTTCTGTG CCTTCAATCTGACGTTCGGGGCTTCCACAGGCCCTGGCTATTGGGACCAACACTACCTCAGCT GGTCGATGCTCCTGGGTGTGGGCTTCCCTCCAGTGGACGGCTTGTCCCCACTAGTCCTGGGCA TGCACCACAAGAAGTACTCAGAGTACCAGTCCATAAATTAAGGCCCGCTCTCTGGAGGGAAGG ACATTACTGAACCTGTCTTGCTGTGCCTCGAAACTCTGGAGGTTGGAGCATCAAGTTCCAGCC GGCCCCTTCACTCCCCCATCTTGCTTTTCTGTGGAACCTCAGAGGCCAGCCTCGACTTCCTGG AGACCCCCAGGTGGGGCTTCCTTCATACTTTGTTGGGGGGACTTTGGAGGCGGGCAGGGGACAG GGCTATTGATAAGGTCCCCTTGGTGTTTGCCTTCTTGCATCTCCACACATTTCCCTTGGATGGG ACTTGCAGGCCTAAATGAGAGGCATTCTGACTGGTTGGCTGCCCTGGAAGGCAAGAAAATAGA TTTATTTTTTTCACAGGGAAAAAAAAAAAA

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FIGURE 66

MRGSVECTWGWGHCAPSPLLLWTLLLFAAPFGLLGEKTRQVSLEVIPNWLGPLQNLLHIRAVG
TNSTLHYVWSSLGPLAVVMVATNTPHSTLSINWSLLLSPEPDGGLMVLPKDSIQFSSALVFTR
LLEFDSTNVSDTAAKPLGRPYPPYSLADFSWNNITDSLDPATLSATFQGHPMNDPTRTFANGS
LAFRVQAFSRSSRPAQPPRLLHTADTCQLEVALIGASPRGNRSLFGLEVATLGQGPDCPSMQE
QHSIDDEYAPAVFQLDQLLWGSLPSGFAQWRPVAYSQKPGGRESALPCQASPLHPALAYSLPQ
SPIVRAFFGSQNNFCAFNLTFGASTGPGYWDQHYLSWSMLLGVGFPPVDGLSPLVLGIMAVAL
GAPGLMLLGGGLVLLLHHKKYSEYQSIN

N-glycosylation sites:

amino acids 65-69, 95-99, 134-138, 159-163, 187-191, 230-234, 333-337

cAMP- and cGMP-dependent protein kinase phosphorylation site: amino acids 397-401

Casein kinase II phosphorylation sites:

amino acids 151-155, 249-253, 255-259

N-myristoylation sites:

amino acids 3-9, 63-69, 235-241, 273-279, 292-298, 324-330

Leucine zipper pattern.

amino acids 371-393

FIGURE 67

CTGGAGAAGGGGTTTCAGCCCCAGGACATTTACTGAGAGTCGGCGAATATTGGGAGCCGCGATGTTCCCCCTTCG GGCCCTGTGGTTGGTCTGGGCGCTTCTAGGAGTGGCCGGATCATGCCCGGAGCCGTGCGCCTGCGTGGACAAGTA GCTTAGTCTGTCCGCGAACAAGATCACTGTGCTGCGGCGCGGGGCCTTCGCCGACGTCACACAGGTCACGTCGCT GTGGCTGGCGCACAATGAGGTGCGCACCGTGGAGCCAGGCGCACTGGCCGTGCTGAGTCAGCTCAAGAACCTCGA TCTGAGCCACAACTTCATATCCAGCTTTCCGTGGAGCGACCTGCGCAACCTGAGCGCGCTGCAGCTGCTCAAAAT GAACCACAACCGCCTGGGCTCTCTGCCCCGGGACGCACTCGGTGCGCTACCCGACCTGCGTTCCCTGCGCATCAA CAACAACCGGCTGCGTACGCTGGCGCCTGGCACCTTCGACGCGCTTAGCGCGCTGTCACACTTGCAACTCTATCA CAATCCCTTCCACTGCGGCTGCGGCCTTGTGTGGCTGCAGGCCTGGGCCGCGAGCACCCGGGTGTCCTTACCCGA TGCACCGCCCAGCGTGCATCTGAGTGCCGAGCCACCGCTTGAAGCACCCGGCACCCCACTGCGCGCAGGACTGGC GTTCGTGTTACACTGCATCGCCGACGGCCACCCTACGCCTCGCCTGCAATGGCAACTTCAGATCCCCGGTGGCAC TGGGGATTTGCTGACGCAGACCCAAGCCCAAACGCCGACTCCAGCACCCGCTTGGCCGGCGCCCCCAGCCACACC CCGTGCACAATGAGCTGGGCGCCAACTCTACGTCAATACGCGTGGCGGTGGCAGCAACCGGGCCCCCAAAACA CGCGCCTGGCGCGGGGGGAGAACCCGACGGACAGGCCCCGACCTCTGAGCGCAAGTCCACAGCCAAGGGCCGGGG CAACAGCGTCCTGCCTTCCAAACCCGAGGGCAAAATCAAAGGCCAAGGCCTGGCCAAGGTCAGCATTCTCGGGGA GACCGAGACGGAGCCGGAGGAGGACACAAGTGAGGGAGAGGAGGCCGAAGACCAGATCCTCGCGGACCCGGCGGA ${\tt GGAGCAGCGCTGTGGCAACGGGGACCCCTCTCGGTACGTTTCTAACCACGCGTTCAACCAGAGCGCAGAGCTCAA}$ ${\tt GCCGCACGTCTTCGAGCTGGGCGTCATCGCGCTGGATGTGGCGGAGCGCGAGGCGCGGGTGCAGCTGACTCCGCT}$ GGCTGCGCGCTGGGCCCTGGGCCCGGCGGGCTGGCGGACCCCGCGACCCGGGCGGCGACCCCTGCGCCTACT GTTTTCCACCAAGAAGGAGCTCCCATCGCTGGTCATAGTGGCAGTGAGCGTATTCCTCCTGGTGCTGGCCAC AGTGCCCCTTCTGGGCGCCGCCTGCTGCCATCTGCTGGCTAAACACCCGGGCAAGCCCTACCGTCTGATCCTGCG GCCTCAGGCCCCTGACCCTATGGAGAAGCGCATCGCCGCAGACTTCGACCCGCGTGCTTCGTACCTCGAGTCCGA GTCCAAGGCCAACCAAGAGGAGTTCGAGGCGGCTCTGAGTACAGCGATCGGCTGCCCCTGGGCGCCGAGGCGGT $\tt CCCGACCTCCACCTAGGGTGCCTGGGAGCAGCAGTCTAGGGCTGGCAGGACTTATGTCCCCCGTCCCCAACCTTC$ ACCTACTCCCCCCTTACTACTCCCCAACCTTGACTACCAGGGACTTCTATTAGGGAGTGGGCCGATTTCACCA GTCCCTGCTACCCACGCTGCCATTCTCCCTGCGGGCTGAATCCCCTTCCCCGCCAAGCACAGTGTTTATCTTAC $\verb|CCCATGCAAGACTCCACCCGCAGACGGTGGGCGATATCTATGTCCCTCCATTCCCGTCGCGATTATCTGCGAAAT| \\$ CCACCCGCAGCCCGCCCCACCGTGGGCTCTGGAGCCAGAGGAAACGAGCGAAGACTTTGGAAACCTCGCGGTAA CGCGGTGGTTTCGGGGGCCAGCCAAGGCCAGTGGAGTGCTGTGGGGTCCCACCTCGACCCCTCCTCCCTTTC CAGGCTGGAGTGCAGTGGCGCATCTCGGCTCACTGCATCTTCCGCCTCCCGGGTTCAAGCGATTCTCCTGCCTC AGCCTGCCTAGTAGCTGGGACTACAGGCGCGCCGCCACCACGACCAGCTAATTTCTTCTATTTTTAGTAGAGACGG GGTTTCACCATGTTGGCCAGGATGGTCTGGATCTCTTGACCTCAGGTGATCCATCTGCCTCGGCCTCTCAAAGTG CTGGGATTACAGGCGTGAGGCACCGCGCCCGGCCCTCCTCCTTTCAATCCCTACTCCCAGAAGCCGGGATTCG TGGCAACCCCTAGTTTTTAGTTCCAAAGCCTCCTGCCGGCAGGGAACCAAATCCTTCTGTCCTCCCACCCCCACC GTTGTTTTCAAAGACAGCGACATTTCGGGTCTGGTGCTAACACCCCCTTCCCAGCCTCTGGGAAAATCGAGTGTG $\verb|CCTTGGCGGCTGAGCCTGTGGACTTGGTCGCGGGCCAATTTCGTTGTCCGTGTTGTTGGGCTTTCCGGAGGTCTGT|\\$ GCGCCCAACAGCGCCGCTCCCGCGGCTCCACCCGACCCTAGCTGGAAAGCGCCGGAGGCGGAGGAAGCT GACTGTGGCCTCCCGGGCCGCGCTCTCTGGAGGGCTCGCGCCCTAGTTCGCACAAAGCCTGCTCGTGACTGTGC CCGCCCCTGCTTCGGCGGGAATCGTGTTTGCCCGGCGTGTAGTCCCTGACAAGCGTGCCCTGTAGGAGAAAAGTC GGAGTTTCAGTCCTCGGGATCAGCCCTCTCCGCGAAGCGCAGCACAAGCGCGGGCCTGGGACGGAGTAGCCCCCC GGAGCCCGTGCCCTTTTCTAAACGCGTCTGTATGCAGTCAATAAAACAATCGATTTGAAA

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FIGURE 68

MFPLRALWLVWALLGVAGSCPEPCACVDKYAHQFADCAYKELREVPEGLPANVTTLSLSANKI
TVLRRGAFADVTQVTSLWLAHNEVRTVEPGALAVLSQLKNLDLSHNFISSFPWSDLRNLSALQ
LLKMNHNRLGSLPRDALGALPDLRSLRINNNRLRTLAPGTFDALSALSHLQLYHNPFHCGCGL
VWLQAWAASTRVSLPEPDSIACASPPALQGVPVYRLPALPCAPPSVHLSAEPPLEAPGTPLRA
GLAFVLHCIADGHPTPRLQWQLQIPGGTVVLEPPVLSGEDDGVGAEEGEGEGDGDLLTQTQAQ
TPTPAPAWPAPPATPRFLALANGSLLVPLLSAKEAGVYTCRAHNELGANSTSIRVAVAATGPP
KHAPGAGGEPDGQAPTSERKSTAKGRGNSVLPSKPEGKIKGQGLAKVSILGETETEPEEDTSE
GEEAEDQILADPAEEQRCGNGDPSRYVSNHAFNQSAELKPHVFELGVIALDVAEREARVQLTP
LAARWGPGPGGAGGAPRPGRRPLRLLYLCPAGGGAAVQWSRVEEGVNAYWFRGLRPGTNYSVC
LALAGEACHVQVVFSTKKELPSLLVIVAVSVFLLVLATVPLLGAACCHLLAKHPGKPYRLILR
PQAPDPMEKRIAADFDPRASYLESEKSYPAGGEAGGEEPEDVQGEGLDEDAEQGDPSGDLQRE
ESLAACSLVESQSKANQEEFEAGSEYSDRLPLGAEAVNIAQEINGNYRQTAG

Important features of the protein:

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 587-610

N-glycosylation sites.

amino acids 52-55, 121-124, 337-340, 364-367, 474-477, 563-566 cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 397-400

Casein kinase II phosphorylation sites.

amino acids 19-23, 202-205, 289-292, 246-249, 411-414, 431-434, 433-436, 440-443, 544-547, 583-586, 650-653, 700-703

N-myristoylation sites.

amino acids 15-20, 48-53, 165-170, 296-301, 351-356, 362-367, 390-395, 419-424, 514-519, 536-541, 557-562, 561-566, 610-615, 661-666, 716-721

Amidation site.

amino acids 522-525

Prokaryotic membrane lipoprotein lipid attachment sites.

amino acids 10-20, 603-613

FIGURE 69

GGCGGCGGAGCGAAGGGGGCGCAGGGATCCTCCAGGCTGCCGGCTGGGAAGGCGTGGG CCATTGCTGAACGGAGAGGTAGCCATGATGCCCCACTTGGTGAATGGAGATGCAGCTCAGCAT GTTATTCTCGTTCAAGTTAATCCAGGTGAGACTTTCACAATAAGAGCAGAGGATGGAACACTT CAGTGCATTCAAGGACCTGCTGAAGTTCCCATGATGTCACCCAATGGATCCATTCCTCCCATT CATGTGCCTCCAGGTTATATCTCACAGGTGATTGAAGATAGTACTGGAGTCCGCCGGGTGGTG GTCACACCCCAGTCTCCTGAGTGTTATCCCCCCAAGCTACCCCTCAGCCATGTCTCCAACCCAT CATCTCCCTCCCTATCTGACTCACCATCCACATTTTATTCATAACTCACACACGGCTTACTAC CCACCTGTTACCGGACCTGGAGATATGCCGCCTCAGTTTTTTCCCCAGCATCATCTTCCCCAC ACAATATATGGTGAGCAAGAAATTATACCATTTTATGGAATGTCAAGCTACATCACCCGAGAA CTCAACAGCCCTCCTTCTTCTATCTACAAAAGCAGCTGCACAACAGTATACAATGGCTATGGG AAGGGCCATAGTGGTGGAAGTGGCGGAGGCGGCAGCGGTAGTGGTCCCGGAATTAAGAAAACA GAGCGACGAGCAAGAAGCAGCCCAAAGTCGAATGATTCAGACTTGCAAGAATATGAGTTGGAA GTAAAGAGGGTGCAAGACATTCTTTCGGGAATAGAGAAACCACAGGTTTCTAATATTCAGGCA AGAGCAGTTGTGTTGTCCTGGGCTCCCCCTGTTGGACTTTCCTGTGGACCCCACAGTGGTCTT TCCTTCCCCTACAGTTACGAGGTGGCCTTATCAGACAAAGGACGAGATGGAAAATACAAGATA ATTTACAGTGGAGAAGAATTAGAATGTAACCTGAAAGATCTTAGACCAGCAACAGATTATCAT GTGAGGGTGTATGCCATGTACAATTCCGTAAAGGGATCCTGCTCCGAGCCTGTTAGCTTCACC ACCCACAGCTGTGCACCCGAGTGTCCTTTCCCCCCTAAGCTGGCACATAGGAGCAAAAGTTCA CTAACCCTGCAGTGGAAGGCACCAATTGACAACGGTTCAAAAATCACCAACTACCTTTTAGAG TGGGATGAGGGAAAAAGAAATAGTGGTTTCAGACAGTGCTTCTTCGGGAGCCAGAAGCACTGC AAGTTGACAAAGCTTTGTCCGGCAATGGGGTACACATTCAGGCTGGCCGCTCGAAACGACATT GGCACCAGTGGTTATAGCCAAGAGGTGGTGTGCTACACATTAGGAAATATCCCTCAGATGCCT TCTGCACCAAGGCTGGTTCGAGCTGGCATCACATGGGTCACGTTGCAGTGGAGTAAGCCAGAA GGCTGTTCACCCGAGGAAGTGATCACCTACACCTTGGAAATTCAGGAGGATGAAAATGATAAC CTTTTCCACCCAAAATACACTGGAGAGGATTTAACCTGTACTGTGAAAAAATCTCAAAAGAAGC CTTGTTTGTACGACGAGTCCTGACAGGCCTGGACCTCCTACCAGACCGCTTGTCAAAGGCCCA GTTACATCTCATGGCTTTAGTGTCAAATGGGATCCCCCTAAGGACAATGGTGGTTCAGAAATC CTCAAGTACTTGCTAGAGATTACTGATGGAAATTCTGAAGGTGAAGTTTTTTGGCAATTGTTTT ATTCAAATCCAA**TAG**CAAGCTCTGTTTTCTAATATAGTAAATGTCTTTATAGTAATAGTGAGT TTTTTCTATTCAAACACAGCACCAGAGATCAGAGTCTACTTGAAACTTACATTTGTGTTATT TTGGTTTGGTTTTTTTTTTTTTTTTGAGATACGATCTCTGTCACACAGGCTGGAGGGC AGTGGCACAGACATGGCCCATTGCAGTCTCAGACTCCTGGGCTTAAGTGACTCTTCTGCCACA GAAGATGAGGAAGAATACATTTTTCATAGTGATGGGGTCTCACTATGTTATCTAGGCTGGTCT CAAACTCCTGGCCTCAAGCAACCCTCCACCTTGGCCTCCCAAAGTGCTGGGACTATAGACATG TGGTATTTTCATCTCCTAACTTGCCATATGTTTTCTGGAAATTCTTATAAGCAGCCGAGAGTG ATCCTGGCCAACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTG GCAGGCACCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGAAGAATTGCTTGAACCCAGCAG GCGGAGGTTGCAGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGTGACAGAGTGAGACTC TGTCTCAAAAAAAAAAA

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FIGURE 70

MMMTDQIPLELPPLLNGEVAMMPHLVNGDAAQHVILVQVNPGETFTIRAEDGTLQCIQGPAEV
PMMSPNGSIPPIHVPPGYISQVIEDSTGVRRVVVTPQSPECYPPSYPSAMSPTHHLPPYLTHH
PHFIHNSHTAYYPPVTGPGDMPPQFFPQHHLPHTIYGEQEIIPFYGMSSYITREDQYSKPPHK
KLKDRQIDRQNRLNSPPSSIYKSSCTTVYNGYGKGHSGGSGGGGSGSGPGIKKTERRARSSPK
SNDSDLQEYELEVKRVQDILSGIEKPQVSNIQARAVVLSWAPPVGLSCGPHSGLSFPYSYEVA
LSDKGRDGKYKIIYSGEELECNLKDLRPATDYHVRVYAMYNSVKGSCSEPVSFTTHSCAPECP
FPPKLAHRSKSSLTLQWKAPIDNGSKITNYLLEWDEGKRNSGFRQCFFGSQKHCKLTKLCPAM
GYTFRLAARNDIGTSGYSQEVVCYTLGNIPQMPSAPRLVRAGITWVTLQWSKPEGCSPEEVIT
YTLEIQEDENDNLFHPKYTGEDLTCTVKNLKRSTQYKFRLTASNTEGKSCPSEVLVCTTSPDR
PGPPTRPLVKGPVTSHGFSVKWDPPKDNGGSEILKYLLEITDGNSEGEVFGNCFIQIQ

Important features of the protein:

N-glycosylation sites.

amino acids 69-73, 254-258, 401-405

Glycosaminoglycan attachment sites.

amino acids 229-233, 234-238, 236-240

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 416-420, 535-539

Tyrosine kinase phosphorylation site.

amino acids 319-326

N-myristoylation sites.

amino acids 52-58, 227-233, 228-234, 230-236, 231-237, 232-238, 235-241, 239-245, 402-408, 610-616

Amidation site.

amino acids 414-418

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 290-301

ATP/GTP-binding site motif A (P-loop).

amino acids 546-554

CUB domain proteins profile.

amino acids 294-301

FIGURE 71

AAGTCATTCAGTGGATGTGATCTTGGCTCACAGGGGACGATGTCAAGCTCTTCCTGGCTCCTTCTCAGCCTTGTT GCTGTAACTGCTCACTCACCATTGAGGAACAGGCCAAGACATTTTTGGACAAGTTTAACCACGAAGCCGAA GACCTGTTCTATCAAAGTTCACTTGCTTCTTGGAATTATAACACCAATATTACTGAAGAGAATGTCCAAAACATG AATAATGCTGGGGACAAATGGTCTGCCTTTTTAAAGGAACAGTCCACACTTGCCCAAATGTATCCACTACAAGAA ATTCAGAATCTCACAGTCAAGCTTCAGCTGCAGGCTCTTCAGCAAAATGGGTCTTCAGTGCTCTCAGAAGACAAG AGCAAACGGTTGAACACAATTCTAAATACAATGAGCACCATCTACAGTACTGGAAAAGTTTGTAACCCAGATAAT CCACAAGAATGCTTATTACTTGAACCAGGTTTGAATGAAATAATGGCAAACAGTTTAGACTACAATGAGAGGGCTC $\tt TGGGCTTGGGAAAGCTGGAGATCTGAGGTCGGCAAGCAGCTGAGGCCATTATATGAAGAGTATGTGGTCTTGAAA$ AATGAGATGGCAAGAGCAAATCATTATGAGGACTATGGGGATTATTGGAGGAGACTATGAAGTAAATGGGGTA GATGGCTATGACTACAGCCGCGGCCAGTTGATTGAAGATGTGGAACATACCTTTGAAGAGATTAAACCATTATAT CCTGCTCATTTGCTTGGTGATATGTGGGGTAGATTTTGGACAAATCTGTACTCTTTGACAGTTCCCTTTGGACAG AAACCAAACATAGATGTTACTGATGCAATGGTGGACCAGGCCTGGGATGCACAGAGAATATTCAAGGAGGCCGAG AAGTTCTTTGTATCTGTTGGTCTTCCTAATATGACTCAAGGATTCTGGGAAAATTCCATGCTAACGGACCCAGGA AATGTTCAGAAAGCAGTCTGCCATCCCACAGCTTGGGACCTGGGGAAGGGCGACTTCAGGATCCTTATGTGCACA AAGGTGACAATGGACGACTTCCTGACAGCTCATCATGAGATGGGGCATATCCAGTATGATATGGCATATGCTGCA CAACCTTTTCTGCTAAGAAATGGAGCTAATGAAGGATTCCATGAAGCTGTTGGGGAAATCATGTCACTTTCTGCA GCCACACCTAAGCATTTAAAATCCATTGGTCTTCTGTCACCCGATTTTCAAGAAGACAATGAAACAGAAATAAAC GTCTTTAAAGGGGAAATTCCCAAAGACCAGTGGATGAAAAAGTGGTGGGAGATGAAGCGAGATAGTTGGGGTG GTGGAACCTGTGCCCCATGATGAAACATACTGTGACCCCGCATCTCTGTTCCATGTTTCTGATGATTACTCATTC ATTCGATATTACACAAGGACCCTTTACCAATTCCAGTTTCAAGAAGCACTTTGTCAAGCAGCTAAACATGAAGGC CCTCTGCACAAATGTGACATCTCAAACTCTACAGAAGCTGGACAGAAACTGTTG**TAA**GAAATACCTCAAAATGTT GAACCTCTCCTAGTATTCAGTATTACTCATTTCCATGCCTAGGTTTTGTATTTGATTTCTTTGTTCTAAAAAAGAAA CGGTTTAGGGTGGAATATATCTGTTAATATGCATTCTTTTCTTATCTGCCAGAAGCAAATTTAGCCAAGTCAAAG AGAAGAAACCATAGATCATAGATGTAAATATATGTACATCTGGAACCCCTCAAAAGGCCCTGAACCCCCTTTTTT TGTGTAGCAATATGCTGAGGCTTGGAAAATCAGAACCCTGGACCCTAGCATTGGAAAATGTTGTAGGAGCAAGAA CATGAATGTAAGGCCACTGCTCAACTACTTTGAGCCCTTATTTACCTGGCTGAAAGACCAGAACAAGAATTCTTT TGTGGGATGGAGTACCGACTGGAGTCCATATGCAGACCCAAAGCATCAAAGTGAGGATAAGCCTAAAATCAGCTC TTGGAGATAAAGCATATGAATGGAACGACAATGAAATGTACCTGTTCCGATCATCTGTTGCATATGCTATGAGGC AGTACTTTTTAAAAGTAAAAATCAGATGATTCTTTTTGGGGAGGAGGATGTGCGAGTGGCTAATTTGAAACCAA GAATCTCCTTTAATTTCTTTGTCACTGCACCTAAAAATGTGTCTGATATCATTCCTAGAACTGAAGTTGAAAAGG ${\tt CCATCAGGATGTCCCGGAGCCGTATCAATGATGCTTTCCGTCTGAATGACAACAGCCTAGAGTTTCTGGGGATAC}$ AGCCAACACTTGGACCTCCTAACCAGCCCCCTGTTTCCATATGGCTGATTGTTTTTGGAGTTGTGATGGGAGTGA TAGTGGTTGGCATTGTCATCCTGATCTTCACTGGGATCAGAGATCGGAAGAAGAAAAATAAAGCAAGAAGTGGAG AAAATCCTTATGCCTCCATCGATATTAGCAAAGGAGAAAATAATCCAGGATTCCAAAACACTGATGATGTTCAGA TAATCTAAATGTAAATGTCTGTTGAATTTCTGAAGTTGAAAACAAGGATATATCATTGGAGCAAGTGTTGGATCT TGTATGGAATATGGATGATCACTTGTAAGGACAGTGCCTGGGAACTGGTGTAGCTGCAAGGATTGAGAATGGCA TGCATTAGCTCACTTTCATTTAATCCATTGTCAAGGATGACATGCTTTCTTCACAGTAACTCAGTTCAAGTACTA CAGGGAACAGGTAGAGGACATTGCTTTTTCACTTCCAAGGTGCTTGATCAACATCTCCCTGACAACACAAAACTA GAGCCAGGGGCCTCCGTGAACTCCCCAGAGCATGCCTGATAGAAACTCATTTCTACTGTTCTCTAACTGTGGAGT ${\tt GAATGGAAATTCCAACTGTATGTTCACCCTCTGAAGTGGGTACCCAGTCTCTTAAATCTTTTGTATTTGCTCACA}$ GTGTTTGAGCAGTGCTGAGCACAAAGCAGACACTCAATAAATGCTAGATTTACAAAA

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FIGURE 72

MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNYNTNITEENVQNMN
NAGDKWSAFLKEQSTLAQMYPLQEIQNLTVKLQLQALQQNGSSVLSEDKSKRLNTILNTMSTI
YSTGKVCNPDNPQECLLLEPGLNEIMANSLDYNERLWAWESWRSEVGKQLRPLYEEYVVLKNE
MARANHYEDYGDYWRGDYEVNGVDGYDYSRGQLIEDVEHTFEEIKPLYEHLHAYVRAKLMNAY
PSYISPIGCLPAHLLGDMWGRFWTNLYSLTVPFGQKPNIDVTDAMVDQAWDAQRIFKEAEKFF
VSVGLPNMTQGFWENSMLTDPGNVQKAVCHPTAWDLGKGDFRILMCTKVTMDDFLTAHHEMGH
IQYDMAYAAQPFLLRNGANEGFHEAVGEIMSLSAATPKHLKSIGLLSPDFQEDNETEINFLLK
QALTIVGTLPFTYMLEKWRWMVFKGEIPKDQWMKKWWEMKREIVGVVEPVPHDETYCDPASLF
HVSDDYSFIRYYTRTLYQFQFQEALCQAAKHEGPLHKCDISNSTEAGQKLL

Important features of the protein:

Signal peptide:

amino acids 1-17

N-glycosylation sites.

amino acids 53-57, 90-94, 103-107, 322-326, 432-438, 546-550

N-myristoylation sites.

amino acids 260-266, 286-292, 395-401

Cell attachment sequence.

amino acids 204-207

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 371-381

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FIGURE 73

GGACGCGGAACTGGTGTACCCTGGTGGACGTGCACCCAGAGGACCAGGCGGCGGCGGCAGGA AGACCTATGCCATGGTGTCCAGCCACTCAGCTGGTCATTCTCTGGCTTCAGAACTGGTGGAGT CCCATGATGGACATGAGGAGATCATTAAGGTGTACTTGAAGGGGAGGTCTGGAGACAAGATGA TTCACGAGAAGATATTAACCAGCTGAAGAGTGAGGTCCAGTACATCCAGGAGGCCAGGAACT GCCTACAGAAGCTCCGGGAGGATATAAGTAGCAAGCTTGACAGGAACCTAGGAGATTCTCTCC ATCGACAGGAGATACAGGTGGTGCTAGAAAAGCCAAATGGCTTTAGTCAGAGTCCCACAGCCC TGTACAGCAGCCCACCTGAGGTGGACACCTGTATAAATGAGGATGTTGAGAGCTTGAGGAAGA CGGTGCAGGACTTGCTGGCCAAGCTTCAGGAGGCCAAGCGGCAACACCAGTCAGACTGTGTGG CTTTTGAGGTCACACTCAGCCGGTACCAGAGGGAAGCAGAACAAAGTAATGTGGCCCTTCAGA GAGAGGAGGACAGATGTCCAGAG<u>TGA</u>TTGGAGAATGTCCTGGGGGAATGAAGTTCCTTCCACA AACACAGCTCAGTTCTTAGCAACAAACTGTTTGTTTTTTCTACTTGCTCCATCTGCAGCCTACG CTGCCCTGGCCTCCTGCAGACAGATAGTGGGGTTACCTGGCAAGGCCTGGTGAGAGCCAGTGA ACCTAAGCTTTGACTGGGTGGCCTTGTCTTTCTGGGGAGGGGAATGTACATTCAGGGAGTA GCCTTTTGCGGAAAAATTCTCTAGGGCTACAGACAGTCATGTGTGACTTCTCTCTGCTGTGAA AACTCCCAGAGTCTCTTTAGGGATTTTCCCTAAGGTGTACCACCAGGCACACCTCAGTCTTCT TGACCCAGAGCCTGAAAACTGTTTTCACTGGGTTCCACCAGTCCCAGCAAAATCCTCTTTGTA TATAGCCTTCTCTTGCAGTATTTGGATTTGCTTGAAACCGGGAAAACTGTTCCCATTAGGCTT GTTAATGTCAGAGTGACACTATTATGAATCTTTCTCTCCCTTTCCTCTGCCTGTTTCTTCTCT CTTTCTCCTTCAAACTTGCTCTGCAGCTAAGGAAGGTGAGTCTACTTTCCCTGAGGCTTTGGG GTCAGAGTATATGTTGTTTGGAGAAAGAGGGCAATCAGGACTCTTCTGGGACCCAGATGAGTT CTTCACTAGCCCTTCTGAACCCCTTGCTCCATAATTGGTCTTTTATCCTGGCTCTGAATGACC CTGTCACCCAGGCTGGAGTGCAGTGGCGCGATCTCAGCTCACTGCAACCTCTGCCTCCCGGAT TTAAGCGATTCTTCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGTGTGCCACCACGCCTG CCTGACCTCAGGTGATCCACCCACCTCGGCTTCCCAAAGTGCTAGGATTATAGGCTTGAGCTA CTGCGCCCGGCCCATGGTGTTTTTCTTTAGGGCTCTTCCTACAGCCTTGAGAAGTAGATAGGC ATCAGAGTATGGTACTATAGGAATCAGAAAATTCAAAACAAATGTGGATTAAGTGTTTAGGC TCTATGTGGCTCACGCAGCCAGAATCCTTAAGTCTGTGTGTTTCTGTGTCTCAAGACTGGGCT CACATTCTGGCTTTGTCCATAACAATGCTCTGGGATTTCAGGGAGTTCCCTCATTTGTAAAAT GAGGGGGTCAGAGCAGGTGATATCCATGTTTCTTCCCTTTCTGATATTGTTGTCTGTGGCATA TTCTTTGTATGGCGAATTTAATAAATTATATTAATGTGTCA

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FIGURE 74

MNGTRNWCTLVDVHPEDQAAAGRKTYAMVSSHSAGHSLASELVESHDGHEEIIKVYLKGRSGD KMIHEKNINQLKSEVQYIQEARNCLQKLREDISSKLDRNLGDSLHRQEIQVVLEKPNGFSQSP TALYSSPPEVDTCINEDVESLRKTVQDLLAKLQEAKRQHQSDCVAFEVTLSRYQREAEQSNVA LQREEDRCPE

Important features of the protein:

Signal peptide:

amino acids 1-39

N-glycosylation site.

amino acids 2-6

Amidation site.

amino acids 21-25

FIGURE 75

GCTTGCACACATGGCTCCGGAGGCTCCGGTTGCCCATCCGAGCCCCTGCCAGGCTCTAACGTTCCCAACTGACAA CACCAGTAACTAAATATAGGAGCAGATGGTGGGGACGGGCTGTCGCAGCGGCTCCTTTGCAGAGGTCTCCGGACT CTGGACCTGGCCGAGTGCAAGCTGGTCTCCTTTCCCATTGGCATCTACAAGGTCCTGCGGAATGTCTCTGGCCAG ATTGACCTGTCCCGGAACCAGTTCCAGGACTTCCCTGAGCAGCTTACCGCCCTGCCGGCGCTGGAGACCATCAAC $\tt CTGGAGGAGAACGAGATCGTAGATGTGCCCGTGGAGAAGCTGGCCGCCATGCCAGCCTTGCGCAGCATCAACCTC$ $\tt CGCTTCAACCCCACTCAACGCCGAGGTGCGCGTGATCGCCCCGCCGCTCATCAAGTTTGACATGCTCATGTCTCCG$ GAAGGCGCAAGAGCCCCCCTACCT**TAG**GCCACCCTCCTCATGCCCAGCCAGCAAGGGACAGAGGCCACAGGCCTG GAACCCTGGAAGGGAGGCCCATGGGAGGCCAAGCCTGGGGGCTGGGGCGGTGGGCCGAGCACGTGG TGGGTGGGGTGCAGCTGGTCTGGATAGATAGCTTACAGCAGTAGTGGGCTCTGGAATGCCCAAGGGAAGAGCCAA GGTGGGGCCTGCAGCCTGGACTCGGCACTCACAGCTGCTGTGCAAACTCAGGCAGATCTCCTGCCCTCTCTGAGC CTTGTCACTTGAAAAAAACAGGACCCTTTCCCTCCTTTGGGCTCCCTGGAGGTTTTTAAGCAGTACGTGCCTCCA AGTTACCTCCAGATCAGCAGGCACAGGTGGGCATTGCCAGGTATTTTCTGAGCCCCTGCGGGTTTGAGGCCTTGT ACCTGGATGCGGCCCTCTGCAGGGCCCAGTCTTCAGTCCTGTGGTCCCTGGACTGGTGGGAACCTGAACTAGGAG TCCTGGGAGAGCTGTGGTGGGAATATGGGCTGGCACTGCTGCAGGGCAAGAACATTCATGTAGGAGCCCGAGGAC CANCANGCTGGGAATGGGGAGCAAGTCACGTCAGCTCTGTCATTCCCCACAGTTAACAAATTGGCGGGGTGGGAA GTCCTGAGTGCTCCGTCCCTCTAGCATCACTCCTGAGCTGCGGGAGAGGTGGCCCAGAGAACAGCAGAGTCAGTT ACACCTGCAGCTCTTGTCTAAAGTGATTAGATGGCCACCCTCACCACTGTCCAGTCCAGCAGCAGCCTGGCTGCC CAAAGCCCTGATGACCTGGTTCTTCTGAGGCCCTCAACCTGGCATCTTAGGGTATGGTCAGGCAACAGGGTGACC ${\tt AGCTGTCCTGGTTTCCCAGGACATGGAACTTTCAATGCTAAAACTGGGACATTACCCAGCAAGTGGGGATGGTTG}$ GTCCCCTACCAGGAGAGGGCCTGGGGCTCTTGCTTCCCGAGAACGCCTGTGGCTTGAAGAACCTTGACTGCTTGG ${\tt TCCTCAGGTATCTACCTCCCACCTTCTCCTCATCTGTGGAGCAAGCCAACTCAGTGCCCCAGACCCCACCTGATC}$ TGCATCTTTGTTTGCTCCAGAGACACCTGAGGCCCCAGAGCTTGAGGCAAAGCCAGGCCGTCCAAATCCTGTGTG CCGTGGACGAGTGGCCACTTTACTACTCCTAAGGCTAAGATGTTGAGAGCTCAGACCACTGCTCAGAGCAGTAAT GCCATTGTTGGGCCATCACTGAGCGCTCAGTATCTCAAGAGACTCTGTTCATTCTGCTCGTATCCCAAGGCCTGG TTGGTCAAACTCTGGGCAAAGGGTTTTCAGGATGAGGAGGTCAAGACAGGATGTCCAGAGCTACCGAGTTCATCT GTGGGTGTTGGGGGCAAGTGGGGGCTGAAGTCCTGTGCAGGCTGGCCCCACCTGCCTTGTGCCCTGGAGT GGGGTTTCTCCTTGTTGAAGAAGAGGCATCCTTCTCTGATGTGCACAAACACAATGTATGACCAGAGCCTTGCAA CTCAAAGTGTGGTCTGTGGACCAGCAGCGGCAGTGACACCTGGGAGCTTGTTAGGAATGCAGAGTCTAGGCCTCA $\verb|CCCTATACCTCCCGACTCAGACCCTGCATTTTAGCAAGACCCCCAGCTGATTCCTATAAGCACTTTAGAGTTTGA|\\$ GAAGCAAGGACCTAGGCTGGGGATGTCCTCCGAGCAGAGGGTGAAGTTTCTCTCAGTTCTCCCTGCCACTTCC AGGGATCTGAGCCTGTGTTCAGCCTCCCTAACCCACCCTGGGAGACACTTGGCCTGTTAGATTGTTCCAGAG TCTGCATGGCACTCCTGAAGAAGGGAGTGTGACCTGCAGTCACCAGGAGATGAGGGTTAGGTGTGCCCAGCCCTC CACAGATGCCCCCAAATCAGAGCTCACAGTGAGTGAGCCCCTAAGCTTCAGTCTGCAATAAAGAATGCATTGGTT ТСААААААААААААААААААААААААААААААААА

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FIGURE 76

MLKKMGEAVARVARKVNETVESGSDTLDLAECKLVSFPIGIYKVLRNVSGQIHLITLANNELK SLTSKFMTTFSQLRELHLEGNFLHRLPSEVSALQHLKAIDLSRNQFQDFPEQLTALPALETIN LEENEIVDVPVEKLAAMPALRSINLRFNPLNAEVRVIAPPLIKFDMLMSPEGARAPLP

Important features of the protein:

N-glycosylation sites.

amino acids 17-21, 47-51

FIGURE 77

 CACCAACAAGCAATCGTTCATGAGAAAGCCGTGCACCCGCTGCAGTTGGGCCATGTGGTCCGCATCGTATTCCAC TAGGTCCCCATTGTACACCAAGTACTGTCCCGGCGTCTCCAGCAGATGCCTGCAGCCTTCCACCTTCTCAAGCAG GGTGGTGTGAGTGCGCTGCTTTCCTTCCTCGCCTGGACCGGAGCCGTCGCGGGAGGCACCCCCGGGGGTGGAGAA GGCTCCGGCGGCAGCAGCAGCAGCAACGTAAGCGGGATGCTCTCCAGGCTGCTTTTCTGCTCGGTCAGCAA ATGGCTGAGCTGGTACATCTCGCTCTCCAGGTAGGAGATCTCGCGGGCCGTCTCTATGAACTGCCGGTAGTTCTG GTAGACGTTGCGCTTCAGGTTCTGCGCCGTCTCCTCCGCCAGCGCCTGGATGCGCTGCCGGTGCTCCTGGAGGTC CCGGTCCCCATCCGACTGCTGCGAGAGCTGCTTCACGTACAGCCGCGCCTCAAAACCCCCTGACTCCAGCTGCCG TCGGCGCCGCAGCCGCCGCCGCTGTCTAGACCCACCCAAGGCCAACCGAGCTCCTGGGCTGAGGAAGCAGGAATG GGAACGAGACGAGTACGCCTGCGCCGGGTCTGAGCGTCAGACACTGCGCCTGCGCAAGTGGGCCGAGCGCAGACA GGCCGAGAGAAATTTCGGTACTGCGCATGAACCGAGCGTGACGTTGAGGTTTGAAATAACCGGCAAAGAGTAAAG GCTGAAACTAGCTTCCTGAAAGCTTCGTAGGGCCCGAGCCCTGTGAGCCCAGGTTCTGCGCCCACTAGGAGGTGT CATGCTGACTGCTTTTTTTAAAGCCCTAGAATCCTTGGCTTCGGCGTTTTGGGGTAAGCTCCGTTCTCGTTCTCAA GCGCGTTTCCGCGAACTCTCGCGGGATTGACGGGCCGTCTCGAGAGCCGGCATCTCCTAGGAGCTAGTCCTGGTC ${\tt GCAACG}$ ATC GATGATGATGTTGGCACTGCGGCTTCAGGAGGAGTGGAACTTGCAGGAGGCGGAGCGCGAT $\tt CATGCCCAGGAGTCCCTGTCGCTAGTGGACGCGTCGTGGGAGTTGGTGGACCCCACACCGGACTTGCAGGCACTG$ TTTGTTCAGTTTAACGACCAATTCTTCTGGGGCCAGCTGGAGGCCGTCGAGGTGAAGTGGAGCGTGCGAATGACC GACAAAGACCGAGAAGGGCATGGTCCAGAATTTTGTAAACATATGCATCGCATCAACAGCCTGACTGGAGCCAAT ATAACGGTATACCATACTTTTCACGATGAGGTGGATGAGTATCGGCGACACTGGTGGCGCTGCAATGGGCCGTGC CAGCACAGGCCACCGTATTACGGCTATGTCAAACGAGCTACTAACAGGGAACCCTCTGCTCATGACTATTGGTGG GGAAAGGCAAAACTAGGAAAGGAACCAGTATTGGCCGCAGAGAATAAAGGTACCTTCGTGTATATTCTTCTGATT GTTTCTGGTGTAGAAGTCTTCAAGTGTAGACTTAAGGAAAAAATCCCACTGTCCATGAAATGATGGTAGGAAAAAC CAGTTTCTTTTTTTCAAAGAAACAAAATTCAATCTCTGATAATATTTGAGGTAAAGTTCCTTTCCCTATCTTGA CTCACTGAGTTATTAGGAAACAGAAGGCAAAAAGATTGTCAAAATAAAAACAATAATTCAAGTAACAATGCCCGG TTCAAAGAATGGGAAAAGGATATGACATATATTTGCCAGTACTTCATCTTCAAGATTTACCCTTTTCCTGTGAAG TTCAGAGTTACTGAAGATGCTTCTTCCCTTGGGAAGTTGTTGACCCAAGAACATAGGTTATATTTCCCAAATCTT TAATTATTGAGTGAAAGAGCTATAGATGAATTGATATGGAAAGACCGTATCTTCATTTTCGTGAGTAGAAGGAAA GATAAGAATGAGGCAGCAGATTTTCCCTCCTGGAATTACACATAAAGGACACTAAGCAATTTTCAAGGTAAATGT CTCTCAATATCAGAACTCCTGAATTCTGAAGATTGCCCTCCTCCCATTAATAGGATTGTATGGATGTAAGATGGA GGCACTTACATAACAATCTTCTTTGCTTTTTTGGCAGATAAACCCAACAGAGGTGAGGCCCAGCTAGTAATCCCT TTTAGTGGGAAAGGATATGTTCTAGGAGAAACAAGCAATTTACCTTCACCTGGGAAACTGATCACTTCACATGCC ATTAATAAAACCCAAGATCTTTTAAATCAAAACCATTCAGCAAATGCTGTAAGACCTAATTCTAAAATCAAGGTG AAATTTGAACAGAATGGTTCAAGTAAAAATTCTCATCTGGTCTCCCCTGCTGTTAGTAACAGTCACCAAAATGTT CTAAGCAACTACTTTCCTAGAGTATCATTTGCCAACCAAAAGGCTTTCAGAGGTGTGAATGGATCTCCAAGGATA AGTGTAACAGTTGGCAACATCCCTAAAAACTCAGTCTCTTCTAGTTCTCAGAGAAGGGTTTCATCTTCTAAGATA TCCCTAAGAAATTCTTCAAAAGTAACGGAATCAGCATCTGTGATGCCATCCCAGGATGTGAGTGGGTCTGAAGAT

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FIGURE 78

MDDDLMLALRLQEEWNLQEAERDHAQESLSLVDASWELVDPTPDLQALFVQFNDQFFWGQLEA VEVKWSVRMTLCAGICSYEGKGGMCSIRLSEPLLKLRPRKDLVETLLHEMIHAYLFVTNNDKD REGHGPEFCKHMHRINSLTGANITVYHTFHDEVDEYRRHWWRCNGPCQHRPPYYGYVKRATNR EPSAHDYWWAEHQKTCGGTYIKIKEPENYSKKGKGKAKLGKEPVLAAENKGTFVYILLIFM

Important features of the protein:

Signal peptide:

amino acids 1-41

N-glycosylation sites.

amino acids 148-151, 217-220

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 184-187

Casein kinase II phosphorylation sites.

amino acids 30-33, 121-124, 154-157, 187-190, 192-195

Tyrosine kinase phosphorylation site.

amino acids 211-218

N-myristoylation sites.

amino acids 59-64, 85-90, 146-151

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 108-117

FIGURE 79

CGGACGCGTGGGTGGCAACCAGGAGAAGCCAAACTTGGTCCCCCGGCTCGCGGAGTGCCTGCG AGCGGTGCTCATGGCGCTCTATGAGGTCTTCTCTCACCCGGTCGAGCGCAGTTACCGCGCGGG GCTCTGCTCCAAAGCCGCGCTGTTCCTGCTGCTGCCGCTGCGCTCACGTACATCCCGCCGCT GCTGGTGGCCTTCCGGAGCCACGGGTTTTGGCTGAAGCGGAGCAGCTACGAGGAGCAGCCGAC CGTGCGCTTCCAACACCAGGTGCTGCTCGTGGCCCTGCTCGGACCCGAAAGCGACGGGTTCCT CGCCTGGAGCACGTTCCCCGCCTTCAACCGGCTGCAAGGGGATCGCCTGCGCGTCCCGCTCGT TTCGACTAGAGAAGAAGACAGGAACCAGGATGGGAAGACGGACATGTTACATTTTAAGCTGGA GCTTCCCCTGCAGTCCACGGAGCACGTTCTCGGTGTGCAGCTCATCCTGACTTTCTCCTATCG ATTACACAGGATGGCGACCCTCGTGATGCAGAGCATGGCGTTTCTCCAGTCCTCCTTTCCTGT CCCGGGATCCCAGTTATACGTGAACGGAGACCTGAGGCTGCAGCAGAAGCAGCCGCTGAGCTG TGGTGGCCTAGATGCCCGATACAACATATCCGTGATCAACGGGACCAGCCCCTTTGCCTATGA CTACGACCTCACCCATATTGTTGCTGCCTACCAGGAGGAACGTTACCACCGTCCTGAATGA TCCCAACCCCATCTGGCTGGTGGGCAGGGCCGCAGATGCTCCATTTGTGATTAATGCTATCAT ${\tt CCGATACCCTGTGGAAGTCATTTCTTATCAGCCAGGATTCTGGGAGATGGTAAAGTTCGCCTG}$ GGTACAGTATGTCAGCATCCTGCTTATCTTCCTCTGGGTGTTTGAAAGAATCAAGATCTTCGT GTTTCAGAATCAGGTGGTGACCACCATTCCTGTGACAGTGACGCCCCGGGGAAGACTTGTGTAA ${\tt GGAGCACTTATCC} \underline{{\tt TAG}} {\tt AAAGGCCATTTCTGAAGACTCAGCAGGACCGTGGCTGCCTCATTGTC}$ ATCTTCTGGGAACATCTTAGGACCTTTTGAAAGAGCCCAGCGGACACCTGCGGGCTTGTGTGC TTTTCCCTCAGAGACAACGGTTCTTTCCGGTTTTGCTCTACACAGTTCCGTATCTTCAGAGCT CCTGCAGAATTGTCAGGGACTAGTTTGTGGAAAGGTCTGAGAGTTCCTGGAGGCTATAATTAG ACATCTTGGAAAGAGTCCCATCTCTGGTCAAGCAGAGACTTTTCCTCTGTTGAACTGAGGAAC ACACTGTGCATTTCTTCTTGTTGTGAGCCACTCTTACTCTTTTCAGGGCTCTCTTGTGAC AAACATGCCAATCACTAGCACTTTGCACCCCTGGGCTTCTCCATTTCCCATTCACAGCTTTGA TTTCCAGAGCTGAGGCCTTTAACTGGAGACCTGGAGGGCCAGGGCCCAAGGGCCAAGGGCCGCA TTAGCACAGGCAATCAGGGAGGGCCGCTGAAGGACACTTGGACCGTCCACCTGCCCCAGCCCA ACAGTCAGTCATCTGTCATCAGCTCAGCTGAGCAGCCCTGGATCTTTGCCGTACTGTGACTGG GCTCTTTGCCCTATTTTTCCCTCTGTCTGTGCCCCTGGATGGCAGGCTGAAGTCAGAGGGGCT GTTTCATTCTCAGCCCCCTCAGCAGCACTGGGGGAAGAAAGCATTGTCACAACAGGTTCTTTC TGGCCCTCACCCAACAGCCTGGGCACTTGGCCCTCCTCCTCCTTGACAGCCCTCCCCCTTCCT GCAAAGGACAGGGGCGACAGGGGTTGGTGTTGGGATTGGCTCCCGCTGCCTGACAACCACAAG TTTATTTGGAAGGCTAGCGGGAAGCCCAGCGGCTGGCGTTTCCCTTGACTAAGGAACAGGGTG CCCATCAGAGTGGGGGGGGCAGCTTTGGGAAGGACACAAGAAGCAGTAAGAGTGTAAAGAGGA TGCTGGCCTGGGCAGGCCAGTCCAGCCTGGCCACTAGCAGAATACCAAGCAGTCCAGTGGATT ACCCTCGTGGCTAAGCAAGTGTCTGCAGGAGCAGAGATGGCTGGAAGGGGCCTCTGCACACGG AAGATGGCTTGTTCAGCCCATTCACCTCCTGAGGATGTGGGCAGTCTCCTCCAAGAACACATG GAGCTGCTTCCTGATCCCAAGCAGGTCATTGCCACTGGAAGGACATGGCCCCGGTGATCCATG CTTCATGCCCACCCAGAAACACACCCCTCAGTGTGTGCCTCAGTTTACTTTGGAGATCAGTTG TCGTTTTTAGTGCTCCTTTAGGCTTACTAAAACAGTTTTGGAAACAAAGCTATTTTGAAGTAT TCAAGCAGAGGAATTCCCTAACACTGACCCCCTTGTCTTTTTTTAATATTCAGGCTGTTTTAT ATGCCTAAATTTTTTTTTTAAGATCTAAACGAAAAATAGTTTCTTGTTTAAATTCACATAAGG CAATGAGATATGGAAAGATGACAAGATACGTATAAACATTGGTTTGCATCTTATTAAATTATT CTAATGCAAATCTTGTATAAAGAACCCATGATGTTTTGTAACTTTCTAATTAAAATGTTCAAA ATGAG

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FIGURE 80

MALYEVFSHPVERSYRAGLCSKAALFLLLAAALTYIPPLLVAFRSHGFWLKRSSYEEQPTVRF
QHQVLLVALLGPESDGFLAWSTFPAFNRLQGDRLRVPLVSTREEDRNQDGKTDMLHFKLELPL
QSTEHVLGVQLILTFSYRLHRMATLVMQSMAFLQSSFPVPGSQLYVNGDLRLQQKQPLSCGGL
DARYNISVINGTSPFAYDYDLTHIVAAYQERNVTTVLNDPNPIWLVGRAADAPFVINAIIRYP
VEVISYQPGFWEMVKFAWVQYVSILLIFLWVFERIKIFVFQNQVVTTIPVTVTPRGDLCKEHLS

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 268-284

N-glycosylation sites.

amino acids 194-198, 199-203, 221-225

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 51-55

Tyrosine kinase phosphorylation site.

amino acids 250-259

N-myristoylation site.

amino acids 187-193

Cell attachment sequence.

amino acids 307-310

FIGURE 81

GCCGGGAGCTTCCCTGATGGTGCCGCCGCCTCCGAGCCGGGGAGGAGCTGCCAGGGGCCAGCTGGGCAGGAGCCT GGGTCCGCTGCTGCTCCTGGCGTTGGGACACACGTGGACCTACAGAGAGGAGCCGGAGGACGGCGACAGAGA AATCTGCTCAGAGAGCAAAATCGCGACGACTAAATACCCGTGTCTGAAGTCTTCAGGCGAGCTCACCACATGCTA CAGGAAAAAGTGCTGCAAAGGATATAAATTTGTTCTTGGACAATGCATCCCAGAAGATTACGACGTTTGTGCCGA GGCTCCCTGTGAACAGCAGTGCACGGACAACTTTGGCCGAGTGCTGTGTTATTCCGGGATACCGATATGA $\verb|CCGGGAGAGCACCGGAAGCGGAGAAGCCATACTGTCTGGATATTGATGAGTGTGCCAGCAGCAATGGGACGCT|\\$ GTGTGCCCACATCTGCATCAATACCTTGGGCAGCTACCGCTGCGAGTGCCGGGAAGGCTACATCCGGGAAGATGA TGGGAAGACATGTACCAGGGGAGACAAATATCCCAATGACACTGGCCATGAGAAGTCTGAGAACATGGTGAAAGC $\tt CGGAACTTGCTGTGCCACATGCAAGGAGTTCTACCAGATGAAGCAGACCGTGCTGCAGCTGAAGCAAAAGATTGC$ $\tt CGGTATGCCAGGCCCTCCTGGGCAGCCCGGCCCACGGGGCTCAATGGGACCCATGGGACCATCTCCTGATCTGTC$ ACCTCAGGAATTTCCCAGCTACCCAGAAGCCATGGACCTGGGCTCTGGAGATGACCATCCAAGAAGAACTGAGAC AAGAGACTTGAGAGCCCCCAGAGACTTCTACCCA<u>TAG</u>CACATCCCAACACCGTCACGCCAAAGGAAGAGAAAGAT TCTTCTCCTGACGTCTCCACTCCTCTTCTTCCAAATACGATGCTATTTTCAGAGTCCCCTCCTAGGCCTGCAG TTTTACATCCTATTTTTCCAGGAACTTTGGATTTAAGTACTCTCACAGTGTCTTAAATCATAAATTCTTGAAGTT AAATTTGGCAGAGTATCAAAAGGGGGAAAATGACAAAGTGAGCTCTAAGAAAATGTGAGCTACTTCTAAGATGT GTGTTCACAATAGACCATAACTCCTCTAGTATCAAAATTGGGGCTCTTCAGTTAAAAAAGGGGTGGGGAGGACAAA CGTGTCGATGTGCTTTGGTGGAGAATTTTTTCCTTGTGCTTCTAGTAGACTTTAAATATTGTATCCCTTTGTCAA ACCTTGTTTCCCAAATTCAATTAAAGAGAGAGAGAATTGAATGGCGTTTAGAGAAGATAGAAAAGAATCACAGT CATATATTTACTGTTATATAGATTGCCACATTCTAAAATTCAAATACGGTGCTTAAGGTTTCATGCCATGCTTAT TAAAACAATGGGCTCTCGTTTGCTATAATATTTTAAAGCTGTTTAATCAACAGTGGAGTCTGCTCTATAAATATA GATTATTTGTTCAATAAACTGGCTGAGCTTAGAGAGAGGTGCAGAATTCCTGGTTCTGAGCAGGTGCCCAGAAGG TACCATTAGGTGCCATGATCCAGGCTGAACCAATATACAGTGGGGCTGAAGTCTGCAAGGAGGTTGCTGGCTTGG GCTGACCTCACTAATGCCATCAGCAGCGGTAGGTAAATTTTTTCTCCTTGGGTATTACAAGTTTTTGTCTGGAGC CAGTTCTTTTAGGCCTTCTCTTTGATTTATTTTCCCCTGCATGTGAGAAGCAGTTCAGAAAAAGGTCTATATCTC CACCTCCTAGTGAGTTAGAGTGTTTTCTCAGAGCACCTCTGGGTGGCAAAGGGAAGCATGTTCCTGCCAAGGTTT GCTGTGGATTCAGAAGCACCAGGAGCAAGAGACCAGAAGGATGATCTGCTCCTTTGTAACGTTGTTGAGGGCCCT CTTGTTTCCAATGAGCAGCTTATAGGTTACTCACAGTCCACTTTCTCACTGGACACACAAAGTGGCTCTTTATCT TCCTGCCATGTCCTTTCCCATTTCTTTTTGGCTTTTTTGCCTCCACCTTTTAGCCCCACATCATTTAACTCCACTA CTGTGAAAGCTTGCTTAAAGAAAATCCCTCTTGGCCGGGTGTGGTAGCCCACGCCTCTAATCCCAGCACTTTGGG ${\tt AGGCTGAGGCGGGGAGATCACAAGGTCAGGAGATCGAGACCAGCCTGACCAACATGGTGAAAACCCTGTCTCTACT}$ AAAAATACAAAAATTAGCTGGGCGTGTTGGCACACACCTGTAATCCCAGCTACTCAGGAGGCTGAGGCAGGAGAA TTACTTTAACCTGCGGGGGGGGCCTAGATTGCGCTACTGCACTCCAGCCTAGGCAACAGAGGGAGACTCTGTCTC ATTAAAAA

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FIGURE 82

MVPPPPSRGGAARGQLGRSLGPLLLLLALGHTWTYREEPEDGDREICSESKIATTKYPCLKSS
GELTTCYRKKCCKGYKFVLGQCIPEDYDVCAEAPCEQQCTDNFGRVLCTCYPGYRYDRERHRK
REKPYCLDIDECASSNGTLCAHICINTLGSYRCECREGYIREDDGKTCTRGDKYPNDTGHEKS
ENMVKAGTCCATCKEFYQMKQTVLQLKQKIALLPNNAADLGKYITGDKVLASNTYLPGPPGLP
GGQGPPGSPGPKGSPGFPGMPGPPGQPGPRGSMGPMGPSPDLSHIKQGRRGPVGPPGAPGRDG
SKGERGAPGPRGSPGPPGSFDFLLLMLADIRNDITELQEKVFGHRTHSSAEEFPLPQEFPSYP
EAMDLGSGDDHPRRTETRDLRAPRDFYP

Important features of the protein:

Signal peptide:

amino acids 1-34

N-glycosylation sites.

amino acids 142-148, 182-188

Tyrosine kinase phosphorylation site.

amino acids 125-132

N-myristoylation sites.

amino acids 10-16, 143-149, 155-161, 196-202, 250-256

Amidation site.

amino acids 299-303

Aspartic acid and asparagine hydroxylation site.

amino acids 150-162

Cell attachment sequence.

amino acids 176-179

Clq domain proteins.

amino acids 247-280

Calcium-binding EGF-like domain proteins pattern proteins.

amino acids 144-165

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FIGURE 83

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FIGURE 84

MKLSGMFLLLSLALFCFLTGVFSQGGQVDCGEFQDPKVYCTRESNPHCGSDGQTYGNKCAFCK AIVKSGGKISLKHPGKC

Important features of the protein:

Signal peptide:

amino acids 1-23

N-myristoylation sites.

amino acids 26-32, 52-58, 56-62, 69-75

Kazal serine protease inhibitors family signature.

amino acids 40-63

FIGURE 85

GGAGCAGACACAGACCCGGGCCGGAGGCCCCTCTTCTAGCCCTGCGGGAACCGGACAGTTC TCGCTCCTGTCATTATGAAAGTGGTCACGCCATTCAATATTAAGACTTGGAGGGAATTGGGGGA AAGAAAGAAGAATCTAAAAGAAGAGAGCGACCGGTGCTTTTAAGGGTGTCTAATTTTCAA AAGAGACGTCTGGGAGTATTTTGCTCTGGGCGTTTGGAGCAACTTCGCGGACAGCGGAGCTCG CCCAGCATGGATGTTCCAGGTTCACAGGCGCCTTTCTTCTGAGAACGACCCTGGCCTTGAAACG TCAGAGCCGGGGACGAAGGCCCCCGGAGGCTGCTGCGAGCTCCGCGCGTTCCTTCGCGCCCTT AGGCGCCCGGCCGGGGCCACTCGGGCTGCGGCTGATGATGCCCGGGCGCCCGGGGGGCGCCTGC CCGCCTGCTGCCGTGCGGGCGCAGAACGACACGGAGCCCATCGTGCTGGAGGGCAAGTGCC TGGTGGTGTGCGACTCCAGCCCGTCGGCGGACGGCGCCGTCACCTCCTCCCTAGGCATCTCCG AGATGAGCAACCGCACCATGACCATCTATTTCGACCAGGTATTAGTAAATATTGGCAACCACT TTGATCTTGCTTCCAGTATATTTGTAGCACCGAGAAAAGGGATTTATAGCTTCAGCTTCCACG TGGTCAAAGTGTATAACAGACAAACCATCCAGGTCAGTTTAATGCAGAATGGCTACCCAGTGA TCTCGGCCTTTGCAGGAGACCAGGATGTCACCAGAGAAGCTGCTAGCAATGGCGTGCTGCTGC TCATGGAAAGGGAAGACAAAGTGCATCTCAAACTTGAGAGAGGCAACCTCATGGGGGGCTGGA AATACTCCACATTCTCGGGCTTCTTGGTGTTTCCTCTA**TAA**ACACAGAGCCCCCTAGATGGTG GGGGAATGGCAAACTGGACCCAGGACTCCGCCCTTTAAAACACCCTGAACTTACTGGAATTGG ACACCTTGTTTCCAACCTCCGTCAGACTGTTGCAGTAGAAGAATGATTTCCTTTGAAACCTCC AGTACTTTTGTTTTTTGGAATACTGACAATTCCTCGGGAACCTGGCCTCTAATTAGT TTTAGATGACAAGGTCTTAAGGAGAAATGAAATTATCGATTTGAGCAATTTGTACCTGTGATT TCGTCCCAACGGAAGGAGACTCCTGACTCCAGGATGGGCTGCAGGTTGCAGTCAGGGCTTGA TATAGCCTTAAGAAAAAGAATGGCTTCACTTTCATTCTGTATTCTTCCCCCCACCATGTGGCT GGGAGGACTTGGGAGGGGGATGGGGACATTGGGAACCTGTCAAGAAGTGCTTTATCCAGAGAA GTATGTTTTGTTTTAGACGAGACCAAACTAAACAAAAAGTATCTGTTTATCAAAGTAAAAGTA ACACAATGGACAATTCTGCTTATTCTCTCAAAGAGATTCTAAGATGCACCTTTAGAACTATTA ATAGCAACCTGCATTTTTTTTTTAATTTATACTTCAGAATCCTTTAAGAACCTGGTGTTCCTGA GTGGTCCTGAATCATATAAGTTGGTAATGGAAGCTGTAATGACCAAGTCCCCTAAACATACTA AGTGAGCGCACAGTGATCAGGTGCTTCAAAGCCAACAGACCAGCTCCTCTTCCTCCGGATCCT CCTGAAAGTCACTGTGGTTAAAGATATTGGTGGAGGTACCCCAGGAGCACTGTTACAAATCCT TCTTGTTTTGGCATCTCGTACAACATTATTAAGACACAGCTGAGAGTTGATGGGTGTGTAATG CATATGCCAAGGAAATGTCACTAATCCCAAAGCAATCAAAAAGGAGACCTCAAACCAGATGTT AATTTGTTCTTTGTGTAACAATGTAACCAAAATATTGATGATAAAAGTCATAATTTAAGATTC

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FIGURE 86

MQAPGRGPLGLRLMMPGRRGALREPGGCGSCLGVALALLLLLLPACCPVRAQNDTEPIVLEGK CLVVCDSSPSADGAVTSSLGISVRSGSAKVAFSATRSTNHEPSEMSNRTMTIYFDQVLVNIGN HFDLASSIFVAPRKGIYSFSFHVVKVYNRQTIQVSLMQNGYPVISAFAGDQDVTREAASNGVL LLMEREDKVHLKLERGNLMGGWKYSTFSGFLVFPL

Important features of the protein:

Signal peptide:

amino acids 1-48

N-glycosylation sites.

amino acids 53-57, 110-114

N-myristoylation sites.

amino acids 26-32, 27-33, 29-35, 33-39, 76-82, 205-211

Amidation site.

amino acids 16-20

Clq domain signature.

amino acids 117-148

Clq domain proteins.

amino acids 115-149

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FIGURE 87

AGGGCCCGCGGTGGAGAGAGCGACGCCCGAGGGGGATCGCCGCAGCGTCCCGGAGCGCCTCTG AGCTGCAGCTGCAGGAGTTCATCAACGAGCGCGGCGTACTGGCCAGTGGGCGGCCTTGCGAGC CCGGCTGCCGGACTTTCTTCCGCGTCTGCCTTAAGCACTTCCAGGCGGTCGTCTCGCCCGGAC CCTGCACCTTCGGGACCGTCTCCACGCCGGTATTGGGCACCAACTCCTTCGCTGTCCGGGACG ACAGTAGCGGGGGGGGGCGCAACCCTCTCCAACTGCCCTTCAATTTCACCTGGCCGGGTACCT TCTCGCTCATCGAAGCTTGGCACGCGCCAGGAGACGACCTGCGGCCAGAGGCCTTGCCAC CAGATGCACTCATCAGCAAGATCGCCATCCAGGGCTCCCTAGCTGTGGGTCAGAACTGGTTAT TGGATGAGCAAACCAGCACCCTCACAAGGCTGCGCTACTCTTACCGGGTCATCTGCAGTGACA ACTACTATGGAGACAACTGCTCCCGCCTGTGCAAGAAGCGCAATGACCACTTCGGCCACTATG TGTGCCAGCCAGATGGCAACTTGTCCTGCCTGCCCGGTTGGACTGGGGAATATTGCCAACAGC CTATCTGTCTTTCGGGCTGTCATGAACAGAATGGCTACTGCAGCAAGCCAGCAGAGTGCCTCT GCCGCCCAGGCTGGCAGGCCGGCTGTGTAACGAATGCATCCCCCACAATGGCTGTCGCCACG GCACCTGCAGCACTCCCTGGCAATGTACTTGTGATGAGGGCTGGGGAGGCCTGTTTTGTGACC AAGATCTCAACTACTGCACCCACCACTCCCCATGCAAGAATGGGGCAACGTGCTCCAACAGTG GGCAGCGAAGCTACACCTGCACCTGTCGCCCAGGCTACACTGGTGTGGACTGTGAGCTGGAGC TCAGCGAGTGTGACAGCAACCCCTGTCGCAATGGAGGCAGCTGTAAGGACCAGGAGGATGGCT ACCACTGCCTGTGTCCTCCGGGCTACTATGGCCTGCACTGTGAACACACCACCTTGAGCTGCG CCGACTCCCCTGCTTCAATGGGGGCTCCTGCCGGGAGCGCAACCAGGGGGCCAACTATGCTT GTGAATGTCCCCCCAACTTCACCGGCTCCAACTGCGAGAAGAAAGTGGACAGGTGCACCAGCA ACCCCTGTGCCAACGGGGGACAGTGCCTGAACCGAGGTCCAAGCCGCATGTGCCGCTGCCGTC CTGGATTCACGGGCACCTACTGTGAACTCCACGTCAGCGACTGTGCCCGTAACCCTTGCGCCC ACGGTGGCACTTGCCATGACCTGGAGAATGGGCTCATGTGCACCTGCCCTGCCGGCTTCTCTG GCCGACGCTGTGAGGTGCGGACATCCATCGATGCCTGTGCCTCGAGTCCCTGCTTCAACAGGG CCACCTGCTACACCGACCTCTCCACAGACACCTTTGTGTGCAACTGCCCTTATGGCTTTGTGG GCAGCCGCTGCGAGTTCCCCGTGGGCTTGCCGCCCAGCTTCCCCTGGGTGGCCGTCTCGCTGG GTGTGGGGCTGCCGGTGCTGCTGCTGCGGCATGGTGGCAGTGGCTGTGCGGCAGCTGC GGCTTCGACGCCGGACGACGCAGCAGGGAAGCCATGAACAACTTGTCGGACTTCCAGAAGG ACAACCTGATTCCTGCCGCCCAGCTTAAAAACACAAACCAGAAGAAGGAGCTGGAAGTGGACT GTGGCCTGGACAAGTCCAACTGTGGCAAACAGCAAAACCACACATTGGACTATAATCTGGCCC CAGGGCCCCTGGGGCGGGGACCATGCCAGGAAAGTTTCCCCACAGTGACAAGAGCTTAGGAG AGAAGGCGCCACTGCGGTTACACAGTGAAAAGCCAGAGTGTCGGATATCAGCGATATGCTCCC CCACGGAGGTA**TAA**GGCAGGAGCCTACCTGGACATCCCTGCTCAGCCCCGCGGCTGGACCTTC CTTCTGCATTGTTTACA

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FIGURE 88

MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCLK
HFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGRNPLQLPFNFTWPGTFSLIIEAWHAPG
DDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCK
KRNDHFGHYVCQPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNE
CIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATCSNSGQRSYTCTCRPG
YTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCR
ERNQGANYACECPPNFTGSNCEKKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCELHV
SDCARNPCAHGGTCHDLENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLSTDTF
VCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREA
MNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGLDKSNCGKQQNHTLDYNLAPGPLGRGTMPGK
FPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 530-552

N-glycosylation sites.

amino acids 108-112, 183-187, 205-209, 393-397, 570-574, 610-614 Glycosaminoglycan attachment site.

amino acids 96-100

Tyrosine kinase phosphorylation site.

amino acids 340-347

N-myristoylation sites.

amino acids 42-48, 204-210, 258-264, 277-283, 297-303, 383-389, 415-421, 461-467, 522-528, 535-541, 563-569, 599-605, 625-631 Amidation site.

amino acids 471-475

Aspartic acid and asparagine hydroxylation site.

amino acids 339-351

EGF-like domain cysteine pattern signature.

amino acids 173-185, 206-218, 239-251, 270-282, 310-322, 348-360, 388-400, 426-438, 464-476, 506-518

Calcium-binding EGF-like:

amino acids 224-245, 255-276, 295-316, 333-354, 373-394, 411-432, 449-470

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FIGURE 89

GTCTCCGCGTCACAGGAACTTCAGCACCCACAGGGCGGACAGCGCTCCCCTCTACCTGGAGAC TTGACTCCCGCGCGCCCCAACCCTGCTTATCCCTTGACCGTCGAGTGTCAGAGATCCTGCAGC CGCCCAGTCCCGGCCCTCTCCCGCCCCACACCCTCCTGGCTCTTCCTGTTTTTACTCC TCCTTTCATTCATAACAAAAGCTACAGCTCCAGGAGCCCAGCGCCGGGCTGTGACCCAAGCC GAGCGTGGAAGA**ATG**GGGTTCCTCGGGACCGGCACTTGGATTCTGGTGTTAGTGCTCCCGATT CAAGCTTTCCCCAAACCTGGAGGAAGCCAAGACAAATCTCTACATAATAGAGAATTAAGTGCA GAAAGACCTTTGAATGAACAGATTGCTGAAGCAGAAGAAGACAAGATTAAAAAAACATATCCT CCAGAAAACAAGCCAGGTCAGAGCAACTATTCTTTTGTTGATAACTTGAACCTGCTAAAGGCA ATAACAGAAAAGGAAAAATTGAGAAAGAAAGACAATCTATAAGAAGCTCCCCACTTGATAAT AAGTTGAATGTGGAAGATGTTGATTCAACCAAGAATCGAAAACTGATCGATGATTATGACTCT ACTAAGAGTGGATTGGATCATAAATTTCAAGATGATCCAGATGGTCTTCATCAACTAGACGGG ACTCCTTTAACCGCTGAAGACATTGTCCATAAAATCGCTGCCAGGATTTATGAAGAAAATGAC AGAGCCGTGTTTGACAAGATTGTTTCTAAACTACTTAATCTCGGCCTTATCACAGAAAGCCAA GCACATACACTGGAAGATGAAGTAGCAGAGGTTTTACAAAAATTAATCTCAAAGGAAGCCAAC AATTATGAGGAGGATCCCAATAAGCCCACAAGCTGGACTGAGAATCAGGCTGGAAAAATACCA GAGAAAGTGACTCCAATGGCAGCAATTCAAGATGGTCTTGCTAAGGGAGAAAACGATGAAACA GTATCTAACACATTAACCTTGACAAATGGCTTGGAAAGGAGAACTAAAACCTACAGTGAAGAC AACTTTGAGGAACTCCAATATTTCCCAAATTTCTATGCGCTACTGAAAAGTATTGATTCAGAA AAAGAAGCAAAAGAAAAAACACTGATTACTATCATGAAAACACTGATTGACTTTGTGAAG ATGATGGTGAAATATGGAACAATATCTCCAGAAGAAGGTGTTTCCTACCTTGAAAACTTGGAT GAAATGATTGCTCTTCAGACCAAAAACAAGCTAGAAAAAAATGCTACTGACAATATAAGCAAG AAGATGGAAAAGGAATATGGAAGCTTGAAGGATTCCACAAAAGATGATAACTCCAACCCAGGA GGAAAGACAGATGAACCCAAAGGAAAAACAGAAGCCTATTTGGAAGCCATCAGAAAAAATATT GAATGGTTGAAGAACATGACAAAAAGGGAAATAAAGAAGATTATGACCTTTCAAAGATGAGA GACTTCATCAATAAACAAGCTGATGCTTATGTGGAGAAAGGCATCCTTGACAAGGAAGAAGCC GAGGCCATCAAGCGCATTTATAGCAGCCTG**TAA**AAATGGCAAAAGATCCAGGAGTCTTTCAAC TGTTTCAGAAAACATAATATAGCTTAAAACACTTCTAATTCTGTGATTAAAATTTTTTTGACCC AAGGGTTATTAGAAAGTGCTGAATTTACAGTAGTTAACCTTTTTACAAGTGGTTAAAACATAGC AAA

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FIGURE 90

MGFLGTGTWILVLVLPIQAFPKPGGSQDKSLHNRELSAERPLNEQIAEAEEDKIKKTYPPENK
PGQSNYSFVDNLNLLKAITEKEKIEKERQSIRSSPLDNKLNVEDVDSTKNRKLIDDYDSTKSG
LDHKFQDDPDGLHQLDGTPLTAEDIVHKIAARIYEENDRAVFDKIVSKLLNLGLITESQAHTL
EDEVAEVLQKLISKEANNYEEDPNKPTSWTENQAGKIPEKVTPMAAIQDGLAKGENDETVSNT
LTLTNGLERRTKTYSEDNFEELQYFPNFYALLKSIDSEKEAKEKETLITIMKTLIDFVKMMVK
YGTISPEEGVSYLENLDEMIALQTKNKLEKNATDNISKLFPAPSEKSHEETDSTKEEAAKMEK
EYGSLKDSTKDDNSNPGGKTDEPKGKTEAYLEAIRKNIEWLKKHDKKGNKEDYDLSKMRDFIN
KQADAYVEKGILDKEEAEAIKRIYSSL

Important features:

N-glycosylation sites:

amino acids 68-71, 346-349, 350-353

Casein kinase II phosphorylation site:

amino acids 70-73, 82-85, 97-100, 125-128, 147-150, 188-191, 217-220, 265-268, 289-292, 305-308, 320-323, 326-329, 362-365, 368-341, 369-372, 382-385, 386-389, 387-390

N-myristoylation sites:

amino acids 143-148, 239-244

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FIGURE 91

TGCATCAGTGCCCAGGCAAGCCCAGGAGTTGACATTTCTCTGCCCAGCC**ATG**GGCCTCACCCT GCTCTTGCTGCTCCTGGGACTAGAAGGTCAGGGCATAGTTGGCAGCCTCCCTGAGGTGCT GCAGGCACCCGTGGGAAGCTCCATTCTGGTGCAGTGCCACTACAGGCTCCAGGATGTCAAAGC TCAGAAGGTGTGGTGCCGGTTCTTGCCGGAGGGGTGCCAGCCCCTGGTGTCCTCAGCTGTGGA GGAAATGGTTACCCTGCAGGAAGAGGATGCTGGCGAGTATGGCTGCATGGTGGATGGGGCCAG GGGGCCCCAGATTTTGCACAGAGTCTCTCTGAACATACTGCCCCCAGAGGAAGAAGAAGAGAC GGAACCCAGCCAGGATGAGAAGAGCATCCCCTTGATCTGGGGTGCTGTGCTCCTGGTAGGTCT GCTGGTGGCAGCGGTGGTGCTGTTTGCTGTGATGGCCAAGAGGAAACAAGAATCCCTCCTCAG TGGTCCACCACGTCAGTGACTCTGGACCGGCTGCTGAATTGCCTTTGGATGTACCACACATTA GGCTTGACTCACCACCTTCATTTGACAATACCACCTACACCAGCCTACCTCTTGATTCCCCAT CAGGAAAACCTTCACTCCCAGCTCCATCCTCATTGCCCCCTCTACCTCCTAAGGTCCTGGTCT GGATCCTTAGGATATCTGAGCAACCAGGGACTTTAAGATCTAATCCAATGTCCTAACTTTACT AGGGAAAGTGACGCTCAGACATGACTGAGATGTCTTGGGGAAGACCTCCCTGCACCCAACTCC CCCACTGGTTCTTCTACCATTACACTGGGCTAAATAAACCCTAATAATGATGTGCAAAAAA

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FIGURE 92

MGLTLLLLLLGLEGQGIVGSLPEVLQAPVGSSILVQCHYRLQDVKAQKVWCRFLPEGCQPLV SSAVDRRAPAGRRTFLTDLGGGLLQVEMVTLQEEDAGEYGCMVDGARGPQILHRVSLNILPPE EEEETHKIGSLAENAFSDPAGSANPLEPSQDEKSIPLIWGAVLLVGLLVAAVVLFAVMAKRKQ ESLLSGPPRQ

Important features of the protein:

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 161-181

N-myristoylation sites.

amino acids 17-23, 172-178

Amidation site.

amino acids 73-79

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FIGURE 93

GGCGGCGTTGCCGGGCTCTCCGGAAGGAGACGTGGCGGCGGTTGGGCCGGTGATACCCGGGCG GGAGTCTGGTCCCGGGCGGGCCGGTGTTACTGGTCCTCTGCGGCCTCCTGGAGGCGTCCGGCG GCGGCCGAGCCCTTCCTCAACTCAGCGATGACATCCCTTTCCGAGTCAACTGGCCCGGCACCG AGTTCTCTCTGCCCACAACTGGAGTTTTATATAAAGAAGATAATTATGTCATCATGACAACTG CACATAAAGAAAAATATAAATGCATACTTCCCCTTGTGACAAGTGGGGATGAGGAAGAAGAAA AGGATTATAAAGGCCCTAATCCAAGAGAGCTTTTGGAGCCACTATTTAAACAAAGCAGTTGTT CCTACAGAATTGAGTCTTATTGGACTTACGAAGTATGTCATGGAAAACACATTCGGCAGTACC ATGAAGAGAAAGTGGTCAGAAAATAAATATTCACGAGTACTACCTTGGGAATATGTTGG CCAAGAACCTTCTATTTGAAAAAGAACGAGAAGCAGAAGAAAAGGAAAAATCAAATGAGATTC CCACTAAAAATATCGAAGGTCAGATGACACCATACTATCCTGTGGGAATGGGAAATGGTACAC CTTGTAGTTTGAAACAGAACCGGCCCAGATCAAGTACTGTGATGTACATATGTCATCCTGAAT CTAAGCATGAAATTCTTTCAGTAGCTGAAGTTACAACTTGTGAATATGAAGTTGTCATTTTGA CACCACTCTTGTGCAGTCATCCTAAATATAGGTTCAGAGCATCTCCTGTGAATGACATATTTT GTCAATCACTGCCAGGATCTCCATTTAAGCCCCTCACCCTGAGGCAGCTGGAGCAGCAGGAAG AAATACTAAGGGTGCCTTTTAGGAGAAATAAAGAGGGTGTCGGTTGGTGGAAATATGAATTCT GCTATGGCAAACATGTACATCAATACCATGAGGACAAGGATAGTGGGAAAACCTCTGTGGTTG TCGGGACATGGAACCAAGAAGAGCATATTGAATGGGCTAAGAAGAATACTGCTAGAGCTTATC ATCTTCAAGACGATGGTACCCAGACAGTCAGGATGGTGTCACATTTTTATGGAAATGGAGATA TTTGTGATATAACTGACAAACCAAGACAGGTGACTGTAAAACTAAAGTGCAAAGAATCAGATT CACCTCATGCTGTTACTGTATATATGCTAGAGCCTCACTCCTGTCAATATATTCTTGGGGTTG AC<u>TAA</u>AGGATATTAAAGTTAGGGGAAAGAAAAGATCATTGAAAGTCATGATAATTTCTGTCCC ACTGTGTCTCATTATAGAGTTCTCAGCCATTGGACCTCTTCTAAAGGATGGTATAAAATGACT CTCAACCACTTTGTGAATACATATGTGTATATAAGAGGTTATTGATAAACTTCTGAGGCAGAC TACTGTGATTCCAAAATAAATCTCATCCAAGCAAGTTAGAGTCCAGCCTAATCAAATGTCATA ATTGTTGTACCTATTGAAAGTTTTTAAATAATAGATTTATTATGTAAATTATGTATATGTAA GTAGCTAATGAAGTAAAGATCATGAAGAAAGAAATTGATAGGTGTAAATGAGAGACCATGTAA AATATGTAAATTCTAGTACCTGAAATCCTTTCAACAGATTTTTATATAGCAACTGCTCTCTGC AAGTAGTTAAACTAGAAACTGGGCACATGGTAGAGGCTCACATGGGAGTTGTCCTCACCCTTG TTCTGAGACTCAGAATGGTTTACTCTAACAAAACACTGTGCTGTCTATCCCTTGTACTTGCCT ATGTCCACAAGCAAAAA

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FIGURE 94

MEEGGGVRSLVPGGPVLLVLCGLLEASGGGRALPQLSDDIPFRVNWPGTEFSLPTTGVLYKE
DNYVIMTTAHKEKYKCILPLVTSGDEEEEKDYKGPNPRELLEPLFKQSSCSYRIESYWTYEVC
HGKHIRQYHEEKETGQKINIHEYYLGNMLAKNLLFEKEREAEEKEKSNEIPTKNIEGQMTPYY
PVGMGNGTPCSLKQNRPRSSTVMYICHPESKHEILSVAEVTTCEYEVVILTPLLCSHPKYRFR
ASPVNDIFCQSLPGSPFKPLTLRQLEQQEEILRVPFRRNKEGVGWWKYEFCYGKHVHQYHEDK
DSGKTSVVVGTWNQEEHIEWAKKNTARAYHLQDDGTQTVRMVSHFYGNGDICDITDKPRQVTV
KLKCKESDSPHAVTVYMLEPHSCQYILGVESPVICKILDTADENGLLSLPN

Important features of the protein:

Signal peptide:

amino acids 1-30

Glycosaminoglycan attachment site.

amino acids 28-32

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 337-341

N-myristoylation sites.

amino acids 6-12, 23-29, 29-35, 49-55, 141-147, 152-158, 192-198, 196-202

Gram-positive cocci surface proteins 'anchoring' hexapeptide. amino acids 54-60

FIGURE 95

TTCCGTTTCTGGGAGGAGTGAGGGGCAACGGGTCGGAGAAAAAGGAAAAAAGAAGGGCTCAGC GCCTCCCGCCGGGCCGTGGACAGAGGGGCACAGTTTCGGCAGGCGGGTGAGGTCGCTGAGGG CCCGCCGGAG<u>ATG</u>TTTTCCTTGTCGAGCACGGTGCAACCCCAGGTTACAGTTCCTCTGAGTCA TCTCATCAATGCCTTCCATACACCAAAAAACACTTCTGTTTCTCTCAGTGGAGTGTCAGTTTC TCAAAACCAGCATCGAGATGTAGTTCCTGAGCATGAGGCTCCCAGCAGTGAGCCTTCACTTAA CTTAAGGGACCTTGGATTATCTGAACTAAAAATTGGACAGATTGATCAGCTGGTAGAAAATCT ACTTCCTGGATTTTGTAAAGGCAAAAACATTTCTTCCCATTGGCATACATCCCATGTCTCTGC ACAATCCTTCTTTGAAAATAAATATGGTAACTTAGATATATTTAGTACATTACGTTCCTCTTG CTTGTATCGACATCATTCAAGAGCTCTTCAAAGCATTTGTTCAGATCTTCAGTACTGGCCAGT TTTCATACAGTCTCGGGGTTTTAAAACTTTGAAATCAAGGACACGACGTCTCCAGTCTACCTC CGAGAGATTAGCTGAAACACAGAATATAGCGCCATCATTCGTGAAGGGGTTTCTTTTGCGGGA CAGAGGATCAGATGTTGAGAGTTTGGACAAACTCATGAAAACCAAAAATATACCTGAAGCTCA CCAAGATGCATTTAAAACTGGTTTTGCGGAAGGTTTTCTGAAAGCTCAAGCACTCACACAAAA AACCAATGATTCCCTAAGGCGAACCCGTCTGATTCTCTTCGTTCTGCTGCTATTCGGCATTTA TGGACTTCTAAAAAACCCATTTTTATCTGTCCGCTTCCGGACAACAACAGGGCTTGATTCTGC AGTAGATCCTGTCCAGATGAAAAATGTCACCTTTGAACATGTTAAAGGGGTGGAGGAAGCTAA ACAAGAATTACAGGAAGTTGTTGAATTCTTGAAAAATCCACAAAAATTTACTATTCTTGGAGG TAAACTTCCAAAAGGAATTCTTTTAGTTGGACCCCCAGGGACTGGAAAGACACTTCTTGCCCG AGCTGTGGCGGAGAAGCTGATGTTCCTTTTTATTATGCTTCTGGATCCGAATTTGATGAGAT GTTTGTGGGTGTGGGAGCCAGCCGTATCAGAAATCTTTTTAGGGAAGCAAAGGCGAATGCTCC TTGTGTTATATTTATTGATGAATTAGATTCTGTTGGTGGGAAGAGAATTGAATCTCCAATGCA AGGAGTTATCATAATAGGAGCCACAAACTTCCCAGAGGCATTAGATAATGCCTTAATACGTCC TGGTCGTTTTGACATGCAAGTTACAGTTCCAAGGCCAGATGTAAAAGGTCGAACAGAAATTTT GAAATGGTATCTCAATAAAATAAAGTTTGATCAATCCGTTGATCCAGAAATTATAGCTCGAGG TACTGTTGGCTTTTCCGGAGCAGAGTTGGAGAATCTTGTGAACCAGGCTGCATTAAAAGCAGC TGTTGATGGAAAAGAAATGGTTACCATGAAGGAGCTGGAGTTTTCCAAAGACAAAATTCTAAT GGGGCCTGAAAGAAGAGTGTGGAAATTGATAACAAAAACAAAACCATCACAGCATATCATGA ATCTGGTCATGCCATTATTGCATATTACACAAAAGATGCCAATGCCTATCAACAAAGCTACAAT CATGCCACGGGGGCCAACACTTGGACATGTCCCTGTTACCTGAGAATGACAGATGGAATGA AACTAGAGCCCAGCTGCTTGCACAAATGGATGTTAGTATGGGAGGAAGAGTGGCAGAGGAGCT TATATTTGGAACCGACCATATTACAACAGGTGCTTCCAGTGATTTTGATAATGCCACTAAAAT AGCAAAGCGGATGGTTACCAAATTTGGAATGAGTGAAAAGCTTGGAGTTATGACCTACAGTGA TACAGGGAAACTAAGTCCAGAAACCCAATCTGCCATCGAACAAGAAATAAGAATCCTTCTAAG GGACTCATATGAACGAGCAAAACATATCTTGAAAACTCATGCAAAGGAGCATAAGAATCTCGC AGAAGCTTTATTGACCTATGAGACTTTGGATGCCAAAGAGATTCAAATTGTTCTTGAGGGGAA AAAGTTGGAAGTGAGA<u>TGA</u>TAACTCTCTTGATATGGATGCTTGCTGGTTTTATTGCAAGAATA TAAGTAGCATTGCAGTAGTCTACTTTTACAACGCTTTCCCCTCATTCTTGATGTGGTGTAATT GAAGGGTGTGAAATGCTTTGTCAATCATTTGTCACATTTATCCAGTTTGGGTTATTCTCATTA TGACACCTATTGCAAATTAGCATCCCATGGCAAATATATTTTGAAAAAATAAAGAACTATCAG GATTGAAAACAAAAAAAAAAA

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FIGURE 96

MFSLSSTVQPQVTVPLSHLINAFHTPKNTSVSLSGVSVSQNQHRDVVPEHEAPSSEPSLNLRD
LGLSELKIGQIDQLVENLLPGFCKGKNISSHWHTSHVSAQSFFENKYGNLDIFSTLRSSCLYR
HHSRALQSICSDLQYWPVFIQSRGFKTLKSRTRRLQSTSERLAETQNIAPSFVKGFLLRDRGS
DVESLDKLMKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDSLRRTRLILFVLLLFGIYGLL
KNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVEEAKQELQEVVEFLKNPQKFTILGGKLP
KGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFVGVGASRIRNLFREAKANAPCVI
FIDELDSVGGKRIESPMHPYSRQTINQLLAEMDGFKPNEGVIIIGATNFPEALDNALIRPGRF
DMQVTVPRPDVKGRTEILKWYLNKIKFDQSVDPEIIARGTVGFSGAELENLVNQAALKAAVDG
KEMVTMKELEFSKDKILMGPERRSVEIDNKNKTITAYHESGHAIIAYYTKDAMPINKATIMPR
GPTLGHVSLLPENDRWNETRAQLLAQMDVSMGGRVAEELIFGTDHITTGASSDFDNATKIAKR
MVTKFGMSEKLGVMTYSDTGKLSPETQSAIEQEIRILLRDSYERAKHILKTHAKEHKNLAEAL
LTYETLDAKEIQIVLEGKKLEVR

Important features of the protein:

Transmembrane domain:

amino acids 238-259

N-glycosylation sites.

amino acids 28-32, 90-94, 230-234, 278-282, 535-539, 584-588, 623-627

N-myristoylation sites.

amino acids 35-41, 266-272, 286-292, 325-331, 357-363, 599-605

Amidation site.

amino acids 387-393, 709-713

ATP/GTP-binding site motif A (P-loop).

amino acids 322-330

AAA-protein family proteins

amino acids 315-336, 343-386, 405-451

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FIGURE 97

GATGGCGCAGCCACAGCTTCTGTGAGATTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGGG GACCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGAGGCTATATGCGTCAATTCCCCAAA CCAGGCCTTACCTGCTGGGCACTAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGCCACG ACCTGTGCCACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTCACGGGAG GCTTGGCAGTTTTTCTTACTCCTGTGGTCTCCAGATTTCAGGCCTAAG**ATG**AAAGCCTCTAGT CTTGCCTTCAGCCTTCTCTCTGCTGCGTTTTATCTCCTATGGACTCCTTCCACTGGACTGAAG ACACTCAATTTGGGAAGCTGTGTGATCGCCACAAACCTTCAGGAAATACGAAATGGATTTTCT GAGATACGGGGCAGTGTGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTAAGGAGGACT GAGTCTTTGCAAGACACAAAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTTGCTAAGACTC TATCTGGACAGGGTATTTAAAAACTACCAGACCCCTGACCATTATACTCTCCGGAAGATCAGC AGCCTCGCCAATTCCTTTCTTACCATCAAGAAGGACCTCCGGCTCTCATGCCCACATGACA TGCCATTGTGGGGAGGAAGCAATGAAGAAATACAGCCAGATTCTGAGTCACTTTGAAAAGCTG GAGACAGAA**TAG**GAGGAAAGTGATGCTGCTGCTAAGAATATTCGAGGTCAAGAGCTCCAGTCT TCAATACCTGCAGAGGAGGCATGACCCCAAACCACCATCTCTTTACTGTACTAGTCTTGTGCT GGTCACAGTGTATCTTATTTATGCATTACTTGCTTCCTTGCATGATTGTCTTTATGCATCCCC AATCTTAATTGAGACCATACTTGTATAAGATTTTTGTAATATCTTTCTGCTATTGGATATATT AAACTTTAAAAAAATTCACAGATTATATTATAACCTGACTAGAGCAGGTGATGTATTTTAT ACAGTAAAAAAAAAACCTTGTAAATTCTAGAAGAGTGGCTAGGGGGGTTATTCATTTGTAT TCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGATATTTGAAATTGAACCAATGAC TACTTAGGATGGGTTGTGGAATAAGTTTTGATGTGGAATTGCACATCTACCTTACAATTACTG

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FIGURE 98

MKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNLQEIRNGFSEIRGSVQAKDGNIDIR ILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTPDHYTLRKISSLANSFLTIKKDLRLC HAHMTCHCGEEAMKKYSQILSHFEKLEPQAAVVKALGELDILLQWMEETE

Signal sequence:

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 107-110, 140-143

N-myristoylation site.

amino acids 51-56

Interleukin 10:

amino acids 9-176

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FIGURE 99

GCGCCGGCTCCGCGCCCCAGTCCGCGGGCCGCGCCGCCGCTCCCGCCGCTCCCGCCG CTCCCGCAGCCGCCCGCCCGCCCGGAGCCCCGCGTCCCTAGGCCTGGCTCCCGCCTGCC CGAGACCCGCCCAGCCTGCCCCGCTCAGCCGCCAGAGAAGATGCGGCTGCTCCCGGAATGGTT CCTCTTGCTCTTTGGCCCGTGGCTCCTTAGGAAGGCCGTCAGTGCCCAGATACCAGAGTCCGG AAGGCCGCAGTACCTGGGGCTGCGCCCGCCGCGGCCGGAGCGGTGCCCCCGGCCAGCAGCT CCCAGAGCCAAGGTCTTCGGACGGCCTAGGCGTGGGCCGCGCCTGGAGCTGGGCCTGGCCGAC CAACCACACGGGGGCGCTGGCCCGGGCAGGGGCAGCCGGGGCGTTGCCCGCGCAGCGCACCAA GAGGAAGCCGTCCATCAAGGCGGCGCGCGCCAAAAAGATCTTCGGCTGGGGGGACTTCTACTT TCGGGTGCATACCCTCAAGTTTTCGCTGCTGGTGACCGGCAAGATCGTGGACCATGTGAACGG TACCTTCAGTGTGTATTTCCGCCACAACTCGTCCAGCCTGGGCAACCTCAGTGTCAGCATCGT GCCGCCTCCAAGCGTGTCGAGTTCGGAGGAGTCTGGCTGCCCGGGCCTGTCCCCCACCCTCT GCAGTCTACGCTCGCCCTGGAGGGGGTGCTTCCTGGGCTGGGGCCCCCGCTGGGGATGGCAGC AGCAGCGGCGGGCCGGGGCTTGGGGGGCTCCCTCGGGGGGCCACTGGCGGGGCCGCTTGGGGG CGCGTTGGGAGTGCCTGGGGCCAAAGAGTCACGCGCTTTCAATTGCCACGTGGAGTATGAGAA GACAAACCGCGCGCGAAGCACCGACCGTGCCTGTACGACCCGTCGCAGGTGTGTTTCACCGA GCACACGCAGAGCCAGGCCGCCTGGCTCTGTGCCAAGCCCTTCAAAGTCATCTGTATCTTCGT CTCTTTCCTCAGCTTTGACTACAAACTGGTGCAGAAGGTGTGCCCAGACTATAACTTCCAGAG ${\tt TGAGCACCCCTACTTCGGA}{\tt TAG}{\tt CGCCCCTCCCCAGCCAGTCCTGAGCCTCCCGCCAAATCCCA}$ GCCTCACTAGGTGGGACCCCCTTCCCAGTGTTCTGCCGCTCCTGTGGCCATGTCGCCCACTCC TTCCACTCTGGGGGCGGAGGGGAATGGCTTCTCGGGACCCTCAGCTAGCGTGGGTGCCCTTTT CCTTATGCGGAGTGCCCGCAAGGCTGGGGTAGCCCCCTCCAGTACACCCCAAAGTGAAAGGGA TAAGAGTGCAGCCCCAGAATAGGCGGGGCTTGGAGGCGGTCCCAATGTCCCCTGGGTCCACAG TGGGTCCCCTTTCACCCTTGGCGCTAGGCTGCGCACTCCCTTTCCCCGCAGCTTTAATAACT CCTGGCCTGGCACCCTCACCCCACCCTGACTTTCCCATCCCCAGCGCTTGTCCTGCTTCACC CATATGCCTGTCCCCTTTTCCTCCAAACCCTATTAGGGTACCGGAAGCAGAACCCCTGGGCTG AGGCCCTGCCCCGGCCCCTGCCCCTGCCCCCCCCCCCCAGTCCAGGCAGTCGAGC TCCACCTGCCCTCTCCTGCTTCCTCCTCGGTGATATTTTTTCTACGCCAAAACAGACGGGA AAAAAAAAAAA

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FIGURE 100

MRLLPEWFLLLFGPWLLRKAVSAQIPESGRPQYLGLRPAAAGAGAPGQQLPEPRSSDGLGVGR
AWSWAWPTNHTGALARAGAAGALPAQRTKRKPSIKAARAKKIFGWGDFYFRVHTLKFSLLVTG
KIVDHVNGTFSVYFRHNSSSLGNLSVSIVPPSKRVEFGGVWLPGPVPHPLQSTLALEGVLPGL
GPPLGMAAAAAGPGLGGSLGGALAGPLGGALGVPGAKESRAFNCHVEYEKTNRARKHRPCLYD
PSQVCFTEHTQSQAAWLCAKPFKVICIFVSFLSFDYKLVQKVCPDYNFQSEHPYFG

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 273-288

N-glycosylation sites.

amino acids 72-76, 133-137, 143-147, 149-153

cAMP- and cGMP-dependent protein kinase phosphorylation site.

N-myristoylation sites.

amino acids 93-97

amino acids 35-41, 58-64, 60-66, 81-87, 84-90, 184-190, 194-200, 203-209, 205-211, 206-212, 209-215, 217-223, 221-227, 224-230

Cytochrome b/b6 Qo site signature.

amino acids 5-11

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FIGURE 101

GCGTCCGGCCTCAGCCCTCTTCCTCCCCATCAGGGGCAGTGCCCACGTCTTTGGAGCTGCAGC GAGGGACGGATGCCGAACCCTCCAGTCCCCTTCAGAGGCGACTGCAACTCGCCCGGCCGTGC CTGGACTCCCTACAGTGGTCCCTACTCTCGTGACTCCCTCGGCCCCTGGGAATAGGACTGTGG ACCTCTTCCCAGTCTTACCGATCTGTGTCTGTGACTTGACTCCTGGAGCCTGCGATATAAATT GCTGCTGCGACAGGGACTGCTATCTTCTCCATCCGAGGACAGTTTTCTCCTTCTGCCTTCCAG GCAGCGTAAGGTCTTCAAGCTGGGTTTGTGTAGACAACTCTGTTATCTTCAGGAGTAATTCCC CGTTTCCTTCAAGAGTTTTCATGGATTCTAATGGAATCAGGCAGTTTTGTGTCCATGTGAACA CTGCAGAGTTTGGAGGCGAATCATTCACTTCAACATTCCAAACTCAATCACCACCATCTTTTT ACAGGGCTGGGGACCCCATTCTTACTTACTTCCCCAAGTGGTCTGTAATAAGCTTGCTGAGAC AACCTGCAGGAGTTGGAGCTGGGGGACTCTGTGCTGAAAGCAATCCTGCAGGTTTCCTAGAGA GTAAAAGTACAACTTGCACTCGTTTTTTCAAGAACCTGGCTAGTAGCTGTACCTTGGATTCAG CCCTCAATGCTGCCTCTTACTATAACTTCACAGTCTTAAAGGTTCCAAGAAGCATGACTGATC CACAGAATATGGAGTTCCAGGTTCCTGTAATACTTACCTCACAGGCTAATGCTCCTCTGTTGG CTGGAAACACTTGTCAGAATGTAGTTTCTCAGGTCACCTATGAGATAGAGACCAATGGGACTT CCTTACAGCAACACTTCATCCTTCGCTTCAGGGCTTTTCAACAGAGCACAGCTGCTTCTCTCA ATATAAGTTACTCAATGACCCTCTTACAGAGCCAGGGTAATGGAAGTTGCTCTGTTAAAAAGAC ATGAAGTGCAGTTTGGAGTGAATGCAATATCTGGATGCAAGCTCAGGTTGAAGAAGGCAGACT GCAGCCACTTGCAGCAGGAGATTTATCAGACTCTTCATGGAAGGCCCAGACCAGAGTATGTTG CCATCTTTGGTAATGCTGACCCAGCCCAGAAAGGAGGGTGGACCAGGATCCTCAACAGGCACT GCAGCATTTCAGCTATAAACTGTACTTCCTGCTGTCTCATACCAGTTTCCCTGGAGATCCAGG TATTGTGGGCATATGTAGGTCTCCTGTCCAACCCGCAAGCTCATGTATCAGGAGTTCGATTCC TATACCAGTGCCAGTCTATACAGGATTCTCAGCAAGTTACAGAAGTATCTTTGACAACTCTTG TGAACTTTGTGGACATTACCCAGAAGCCACAGCCTCCAAGGGGCCAACCCAAAATGGACTGGA AATGGCCATTCGACTTCTTTCCCTTCAAAGTGGCATTCAGCAGAGGAGTATTCTCTCAAAAAAT GCTCAGTCTCTCCCATCCTTATCCTGTGCCTCTTACTACTTGGAGTTCTCAACCTAGAGACTA TG<u>TGAAGAAAAGAAAATAATCAGATTTCAGTTTTCCCTATGAGAAACTCTGAGGCAGCCACT</u>T ATCTTGGCTAAATAGAACCTCACCTGCTCATGACCAGAGAGCATTTAGGATAATAGATGACCT AACTGAAGGAATCCTTGTATATGAAAGGAGTTATTTTAGAAAAGCAATAAAAATATTTTATTC ATCNTAAAAAAAAA

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FIGURE 102

MRTPQLALLQVFFLVFPDGVRPQPSSSPSGAVPTSLELQRGTDGGTLQSPSEATATRPAVPGL
PTVVPTLVTPSAPGNRTVDLFPVLPICVCDLTPGACDINCCCDRDCYLLHPRTVFSFCLPGSV
RSSSWVCVDNSVIFRSNSPFPSRVFMDSNGIRQFCVHVNNSNLNYFQKLQKVNATNFQALAAE
FGGESFTSTFQTQSPPSFYRAGDPILTYFPKWSVISLLRQPAGVGAGGLCAESNPAGFLESKS
TTCTRFFKNLASSCTLDSALNAASYYNFTVLKVPRSMTDPQNMEFQVPVILTSQANAPLLAGN
TCQNVVSQVTYEIETNGTFGIQKVSVSLGQTNLTVEPGASLQQHFILRFRAFQQSTAASLTSP
RSGNPGYIVGKPLLALTDDISYSMTLLQSQGNGSCSVKRHEVQFGVNAISGCKLRLKKADCSH
LQQEIYQTLHGRPRPEYVAIFGNADPAQKGGWTRILNRHCSISAINCTSCCLIPVSLEIQVLW
AYVGLLSNPQAHVSGVRFLYQCQSIQDSQQVTEVSLTTLVNFVDITQKPQPPRGQPKMDWKWP
FDFFPFKVAFSRGVFSQKCSVSPILILCLLLLGVLNLETM

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domains:

amino acids 484-505, 581-600

N-glycosylation sites.

amino acids 78-82, 165-169, 179-185, 279-285, 331-337, 347-351, 410-414, 487-491

N-myristoylation sites.

amino acids 30-36, 41-47, 124-130, 232-238, 236-242, 409-415

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 420-431

FIGURE 103

CCTAATTCTCAAGGTGATGCTATTTAGGAAGTCATAACTCATGTGAGTGGAGCCATGTGGGAT TAAGAAGTGATAGGAGAGCTTGCTGTCTGTCTCTCTCCACTGTGTGAGGATACAACAGGA AGACAGCCATCTGGTGAGGAAGAGGGGCCCTCGCCAGATACCGGACCTGCTGACACCTTGAT CTTGGACTTCCCATCTTCCAGGAAGGCCTGACCTCAGTTGTTCCAGGGTAAAGAATTTGGGCA GTGCCCACACCCACGCTGTTGGATAACATTTCTTCACCATACCAGTGAGGGTGAATGTGTACA CGCCCAGCTTCCTGCCTGTTACTCTCCACAGT**ATG**CGAAGAATATCCCTGACTTCTAGCCCTG CTCTTTGCTTCAACTTCACTATAAAATCATTGTCCAGACCTGGACAGCCCTGGTGTGAAGCGC AGGTCTTCTTGAATAAAATCTTTTCCTTCAGTACAACAGTGACAACATGGTCAAACCTC TGGGCCTCCTGGGGAAGAAGGTATATGCCACCAGCACTTGGGGAGAATTGACCCAAACGCTGG GAGAAGTGGGGCGAGACCTCAGGATGCTCCTTTGTGACATCAAACCCCAGATAAAGACCAGTG ATCCTTCCACTCTGCAAGTCGAGATGTTTTGTCAACGTGAAGCAGAACGGTGCACTGGTGCAT CCTGGCAGTTCGCCACCAATGGAGAGAAATCCCTCCTCTTTGACGCAATGAACATGACCTGGA AGTATTTCAGGAAGCTCTCAAAGGGAGACTGCGATCACTGGCTCAGGGAATTCTTAGGGCACT GGGAGGCAATGCCAGAACCGACAGGCAGAAGATCCACC**TAG**AGGTGATACCACGGCGGCGCAG AGTTGTTCACCTGTGGTCCTCGATCGCTGACAGCCTTGGCTCCCACTGCTGTGTTCCCTGA GTCAAGTGGAGGCGGAGCCTGCAATGAGCGGAGATCGCGCCTCTGCATTCCAGTCTTGGCAAC AGAGCAAGACTCCGTCTCAAAAAAAAAATTTTTTTTTCAGTACATATTTTTTAAAAAGATAGG GCTGGGCACAGCTCACATCTATAATCCCAACACTTTGGGAGGCCTAGGCAGGAGGATCAC TTGAGCCCAGGAATCTGAAGCTGCAGTGAGCCTTTGCTCGTGAGATTGTGGACCTATGATCCT ACCACCAGCCCACCTGGTTCTAACACCCCCTCCTCTATGTGTGAGAGGGAGAGAAAAAGTG AGGGAGAAAAGAGAGATAAGCAAAGAACAGAGAGGAAAAATGGAAAATAAGAGGAAATTGGGG GAATTAAACAGAGGGGAGGCATGGATCCCCGGGAGTTAGAAGAGTAGCAGCTTGTGGATTAC CAGTTTTCTGCATTCACCATTTCTCACAGACTAAGTTACTCATAAGCAAACGTGCAATTCACA TTACACTGAAATTCTTCCCTAATACATCATTTGCATTGGAATAAAGTACGGTTTTCAAACAAC TGTTTGTTTTTTGAGACAGAGTCTCACTCTATCTCCCAGGCTGGAGTGTAGTGGTGCGATCC CGGCTCACTGCAACCTCGATCTCCCAGGCTCAAGCGATTCCCCTGCCTCAGCCTCCTGAGTAG CTGGGATTACAGGCATGAGCCACCACGCCCGGCTAATTTTTGTATTTTTAGTAGAGACGGGGT TTCACCCTGTTGGCCAGGCTGGTCTCGAACTACGGACCTCAGGTGATCTGCCCCCCTCAGCCT ACACTTTAACACTGAATGCA

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FIGURE 104

MRRISLTSSPVRLLLFLLLLIALEIMVGGHSLCFNFTIKSLSRPGQPWCEAQVFLNKNLFLQ YNSDNNMVKPLGLLGKKVYATSTWGELTQTLGEVGRDLRMLLCDIKPQIKTSDPSTLQVEMFC QREAERCTGASWQFATNGEKSLLFDAMNMTWTVINHEASKIKETWKKDRGLEKYFRKLSKGDC DHWLREFLGHWEAMPEPTGRRST

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 11-30 (possible type II protein)

N-glycosylation site.

amino acids 36-39, 154-157

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 2-5, 182-185, 209-212

Casein kinase II phosphorylation site.

amino acids 86-89, 93-96, 142-145, 185-188

N-myristoylation site.

amino acids 46-51

Amidation site.

amino acids 77-80, 207-210

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FIGURE 105

TTTTCCGAGTGACCTTCTTG**ATG**CTGGCTGTTTCTCTCACCGTTCCCCTGCTTGGAGCCATGA GTGTTCTGCATCCAAATACGAAGCTGCGACAGGCAGAAAGGCTGTTTGAAAATCAACTTGTTG GACCGGAGTCCATAGCACATATTGGGGATGTGATGTTTACTGGGACAGCAGATGGCCGGGTCG TAAAACTTGAAAATGGTGAAATAGAGACCATTGCCCGGTTTGGTTCGGGCCCTTGCAAAACCC GAGATGATGAGCCTGTGTGTGGGAGACCCCTGGGTATCCGTGCAGGGCCCAATGGGACTCTCT TTGTGGCCGATGCATACAAGGGACTATTTGAAGTAAATCCCTGGAAACGTGAAGTGAAACTGC TGCTGTCCTCCGAGACACCCATTGAGGGGAAGAACATGTCCTTTGTGAATGATCTTACAGTCA CTCAGGATGGGAGGAAGATTTATTTCACCGATTCTAGCAGCAAATGGCAAAGACGAGACTACC TGCTTCTGGTGATGGAGGGCACAGATGACGGGCGCCTGCTGGAGTATGATACTGTGACCAGGG AAGTAAAAGTTTTATTGGACCAGCTGCGGTTCCCGAATGGAGTCCAGCTGTCTCCTGCAGAAG ACTTTGTCCTGGTGGCAGAAACAACCATGGCCAGGATACGAAGAGTCTACGTTTCTGGCCTGA TGAAGGGCGGGCTGATCTGTTTGTGGAGAACATGCCTGGATTTCCAGACAACATCCGGCCCA GCAGCTCTGGGGGGTACTGGGTGGGCATGTCGACCATCCGCCCTAACCCTGGGTTTTCCATGC TGGATTTCTTATCTGAGAGACCCTGGATTAAAAGGATGATTTTTAAGCTCTTTAGTCAAGAGA CGGTGATGAAGTTTGTGCCGCGGTACAGCCTCGTCCTAGAACTCAGCGACAGCGGTGCCTTCC GGAGAAGCCTGCATGATCCCGATGGGCTGGTGGCCACCTACATCAGCGAGGTGCACGAACACG ATGGGCACCTGTACCTGGGCTCTTTCAGGTCCCCCTTCCTCTGCAGACTCAGCCTCCAGGCTG TTTAGCCCTCCCAGATAGCTGCCCCTGCCACGCAGGCCAGGAGTCTTCACACTCAGGCACCAG GCCTGGTCCAGGAGGAGCTGTGGACACAGTCGTGGTTCAAGTGTCCACATGCACCTGTTAGTC CCTGAGAGGTGGTGGGAATGGCTGCTTCATTCCTCGAGGATGCCCGGGCCCCACCTGGGCTTG TCTTTCTGTTTAGAGGGAAGTGTAACATATCTGCCATGAGGAACATAAATTCATGTAAAGCCA TTTTCTCTTAAACAAAACAAACTTTCTAAGTACAATCATTCTCTAGGATTTGGGAAGCTCCT TGCACTTGGAACAGGGCTCAGGTGGGTGGAGCAGTAAGGCACTACCCAGAGAGCTTGCTGCTG CGGCCCTGTCCTGCGGCCTCAAAGTTCTTCTTTACTATATAACGTGCGGTCATACCTTTCT TCGTTGTGGTGGGATGGAAGAGCAGGGGAGCATGGCCCAGGGGTGTTGAGGCCAGCGGTGA GAGCCGTGTTAGCCAAGACATGGAACTGTGTTCTCAAGGGTTATGTGGGGCGTGGGCTCTCCA GTGAATATCTCCGTGCTGACCATGCTGGAATTGGATGATTCTGCAATTCGGGACCTACTGCAG GGGTCCGTTTAGTAACGTCTTGTCTGTGATCTTTGTTCTTGACCTCTAGACCCCAAGATGTGA ACAGTGCACGTGTTAATGTCATCTTTGCTCATGTGTTATAAGCCCCAAGTTGCTGTATATTTT CACAAGTATGTCTACACACTGG

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FIGURE 106

MLAVSLTVPLLGAMMLLESPIDPQPLSFKEPPLLLGVLHPNTKLRQAERLFENQLVGPESIAH IGDVMFTGTADGRVVKLENGEIETIARFGSGPCKTRDDEPVCGRPLGIRAGPNGTLFVADAYK GLFEVNPWKREVKLLLSSETPIEGKNMSFVNDLTVTQDGRKIYFTDSSSKWQRRDYLLLVMEG TDDGRLLEYDTVTREVKVLLDQLRFPNGVQLSPAEDFVLVAETTMARIRRVYVSGLMKGGADL FVENMPGFPDNIRPSSSGGYWVGMSTIRPNPGFSMLDFLSERPWIKRMIFKLFSQETVMKFVPRYSLVLELSDSGAFRRSLHDPDGLVATYISEVHEHDGHLYLGSFRSPFLCRLSLQAV

Important features of the protein:

Signal peptide:

amino acids 1-13

Transmembrane domain:

amino acids 1-21 (possible type II)

N-glycosylation sites.

amino acids 116-119, 152-155

Casein kinase II phosphorylation sites.

amino acids 19-22, 27-30, 98-101, 146-149, 221-224, 286-289, 332-335

N-myristoylation sites.

amino acids 71-76, 92-97, 189-194, 244-249, 338-343

Amidation site.

amino acids 164-167

FIGURE 107

CAGGCCTGAGCTGCCCTCCCACTGCCTTTCCTTCTTCCCGCGAGTCAGAAGCTTCGCGAGGG CCCGCGCCCCAGGAAACCGCCGGCGTTCGGCGCTGCGCAGAGCC**ATG**GAATTCTCCTGGCTGG AGACGCGCTGGGCGCCCTTTTACCTGGCGTTCGTGTTCTGCCTGGCCCTGGGGCTGCTGC AGGCCATTAAGCTGTACCTGCGGAGGCAGCGGCTGCTGCGGGACCTGCGCCCCTTCCCAGCGC CCCCCACCCACTGGTTCCTTGGGCACCAGAAGTTTATTCAGGATGATAACATGGAGAAGCTTG AGGAAATTATTGAAAAATACCCTCGTGCCTTCCCTTTCTGGATTGGGCCCTTTCAGGCATTTT TCTGTATCTATGACCCAGACTATGCAAAGACACTTCTGAGCAGAACAGATCCCAAGTCCCAGT ACCTGCAGAAATTCTCACCTCCACTTCTTGGAAAAGGACTAGCGGCTCTAGACGGACCCAAGT GGTTCCAGCATCGTCGCCTACTAACTCCTGGATTCCATTTTAACATCCTGAAAGCATACATTG AGGTGATGGCTCATTCTGTGAAAATGATGCTGGATAAGTGGGAGAAGATTTGCAGCACTCAGG ACACAAGCGTGGAGGTCTATGAGCACATCAACTCGATGTCTCTGGATATAATCATGAAATGCG CTTTCAGCAAGGAGACCAACTGCCAGACAAACAGCACCCATGATCCTTATGCAAAAGCCATAT TTGAACTCAGCAAAATCATATTTCACCGCTTGTACAGTTTGTTGTATCACAGTGACATAATTT TCAAACTCAGCCCTCAGGGCTACCGCTTCCAGAAGTTAAGCCGAGTGTTGAATCAGTACACAG ATACAATAATCCAGGAAAGAAAGAAATCCCTCCAGGCTGGGGTAAAGCAGGATAACACTCCGA AGAGGAAGTACCAGGATTTTCTGGATATTGTCCTTTCTGCCAAGGATGAAAGTGGTAGCAGCT TCTCAGATATTGATGTACACTCTGAAGTGAGCACATTCCTGTTGGCAGGACATGACACCTTGG CAGCAAGCATCTCCTGGATCCTTTACTGCCTGGCTCTGAACCCTGAGCATCAAGAGAGATGCC GGGAGGAGGTCAGGGGCATCCTGGGGGGATGGGTCTTCTATCACTTGGGACCAGCTGGGTGAGA TGGTTCTTAGTATTTGGGGTCTTCACCACACCCTGCTGTCTGGAAAAACCCAAAGGTCTTTG ACCCCTTGAGGTTCTCTCAGGAGAATTCTGATCAGAGACACCCCTATGCCTACTTACCATTCT CAGCTGGATCAAGGAACTGCATTGGGCAGGAGTTTGCCATGATTGAGTTAAAGGTAACCATTG CCTTGATTCTGCTCCACTTCAGAGTGACTCCAGACCCCACCAGGCCTCTTACTTTCCCCAACC ATTTTATCCTCAAGCCCAAGAATGGGATGTATTTGCACCTGAAGAAACTCTCTGAATGT<u>TAG</u>A TCTCAGGGTACAATGATTAAACGTACTTTGTTTTTCGAAGTTAAATTTACAGCTAATGATCCA AGCAGATAGAAAGGGATCAATGTATGGTGGGAGGATTGGAGGTTGGTGGGATAGGGGTCTCTG TGAAGAGATCCAAAATCATTTCTAGGTACACAGTGTGTCAGCTAGATCTGTTTCTATAAACT TTGGGAGATTTTCAGATCTTTTCTGTTAAACTTTCACTACTATTAATGCTGTATACACCAATA GACTTTCATATATTTTCTGTTGTTTTTTAAAATAGTTTTCAGAATTATGCAAGTAATAAGTGCA TGTATGCTCACTGTCAAAAATTCCCAACACTAGAAAATCATGTAGAATAAAAATTTTAAATCT CACTTCACTTAGCCGACATTCCATGCCCTGACCAATCCTACTGCTTTTCCTAAAAACAGAATA ATTTGGTGTGCATTCTTTCAGACTTTTTCCTATACATTTTATATGTAGAAATGTAGCAATGTA TTTGTATAGATGTGATCATTCCTATATTGTTATTGATTTTTTTCACTTAATAAAAATTCACCT TATTCCTTAAAA

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FIGURE 108

MEFSWLETRWARPFYLAFVFCLALGLLQAIKLYLRRQRLLRDLRPFPAPPTHWFLGHQKFIQD
DNMEKLEEIIEKYPRAFPFWIGPFQAFFCIYDPDYAKTLLSRTDPKSQYLQKFSPPLLGKGLA
ALDGPKWFQHRRLLTPGFHFNILKAYIEVMAHSVKMMLDKWEKICSTQDTSVEVYEHINSMSL.
DIIMKCAFSKETNCQTNSTHDPYAKAIFELSKIIFHRLYSLLYHSDIIFKLSPQGYRFQKLSR
VLNQYTDTIIQERKKSLQAGVKQDNTPKRKYQDFLDIVLSAKDESGSSFSDIDVHSEVSTFLL
AGHDTLAASISWILYCLALNPEHQERCREEVRGILGDGSSITWDQLGEMSYTTMCIKETCRLI
PAVPSISRDLSKPLTFPDGCTLPAGITVVLSIWGLHHNPAVWKNPKVFDPLRFSQENSDQRHP
YAYLPFSAGSRNCIGQEFAMIELKVTIALILLHFRVTPDPTRPLTFPNHFILKPKNGMYLHLK
KLSEC

Important features of the protein:

Signal peptide:

amino acids 1-29

Transmembrane domains:

amino acids 310-330, 397-413, 459-473

N-glycosylation site.

amino acids 206-210

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 265-269, 504-520

N-myristoylation sites.

amino acids 25-31, 298-304, 353-359, 450-456, 456-462

Cytochrome P450 cysteine heme-iron ligand signature.

amino acids 447-457

Cytochrome P450 cysteine heme-iron ligand proteins.

amino acids 444-475

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FIGURE 109

GGCGTTCCGGGCCTCAACTTTGGCGTCGTGAGATTCTTGTGAGGCGTCTGCCTGGAAGCCGGC AGCAATTTTGCTTCTTTAAAGAGAAAAAGAAGGCTAGGGACTCAGATTCCTGGATTCTGAGAT CCAGACCAGCTCCTCCAGACCTCTCCAGAAGAAGCCATGGGAACCCCTCGTATCCAGCATTT GCTGATCCTCCTGGTCCTAGGAGCCTCCCTCCTGACCTCGGGCCTAGAGCTGTATTGTCAAAA GGGTCTGTCCATGACTGTGGAAGCAGATCCAGCCAATATGTTTAACTGGACCACAGAGGAAGT GGAGACTTGTGACAAAGGGGCACTTTGCCAGGAAACCATACTAATAATTAAAGCAGGGACTGA GACAGCCATTTTGGCCACGAAGGGCTGCATCCCGGAAGGGGAGGAGGCCATAACAATTGTCCA GCACTCTTCACCTCCCGGCCTGATCGTGACCTCCTACAGTAACTACTGTGAGGATTCCTTCTG TAATGACAAAGACAGCCTGTCTCAGTTTTGGGAGTTCAGTGAGACCACAGCTTCCACTGTGTC AACAACCCTCCATTGTCCAACCTGTGTGGGCTTTGGGGACCTGTTTCAGTGCTCCTTCTCTCC CTGTCCCAATGGTACAACTCGATGCTATCAAGGAAAACTTGAGATCACTGGAGGTGGCATTGA GTCGTCTGTGGAGGTCAAAGGCTGTACAGCCATGATTGGCTGCAGGCTGATGTCTGGAATCTT GACTGAAAATGGGGCCACCTGTCTTCCCATTCCTGTTTGGGGGTTACAGCTACTGCTGCCATT GCTGCTGCCATCATTTATTCACTTTTCC**TAA**GAAGGCACTTCTGGGCCTGGGTCTGAGGACAT CTTTTTTGACTGGGAGCCTTCTTACTGTTGAGGTTCAACAAGCTGAGGAGTAGATGGGAATTT GAGGGAGAATACAGAGATACTATGAACGTATTTGACATTTTTAATACAATTTCTGCTATAATT TTTGTATGCAGTAGGCGTTACTAATAAACATTTCTGCTGTGA

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FIGURE 110

MGTPRIQHLLILLVLGASLLTSGLELYCQKGLSMTVEADPANMFNWTTEEVETCDKGALCQET ILIIKAGTETAILATKGCIPEGEEAITIVQHSSPPGLIVTSYSNYCEDSFCNDKDSLSQFWEF SETTASTVSTTLHCPTCVALGTCFSAPSLPCPNGTTRCYQGKLEITGGGIESSVEVKGCTAMI GCRLMSGILAVGPMFVREACPHQLLTQPRKTENGATCLPIPVWGLQLLLPLLLPSFIHFS

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 184-201

N-glycosylation sites.

amino acids 45-49, 159-163

N-myristoylation sites.

amino acids 31-37, 70-76, 99-105, 147-153, 160-166, 174-180, 175-181

FIGURE 111

CGAGAAGAGGACAGAGGAGACTGAGCAAAGGGGGGTGGGCTCCAGGCGACCCCTAGCCCAATTCTGCCCCTCCAT $\texttt{TGAGTCGCC} \underline{\textbf{ATG}} \texttt{GGGACTCCCAGGGCCCAGCACCCGCCGCCTCCCCAGCTGCTGTTCCTAATTCTGCTGAGCTGT}$ CCCTGGATCCAGGGTCTGCCCCTGAAGGAGGAGGAGATATTGCCAGAGCCTGGAAGTGAGACCCCCACGGTGGCC TCTGAGGCCCTGGCTGAACTGCTTCATGGGGCCCTGCTGAGGAGGGGCCCAGAGATGGGCTACCTGCCAGGATCT $\tt CCGGGGACAGGGCCTCTGACAACAGCCGTCACCCCTAACGGGGTCAGGGGGGCAGGCCCCACTGCGCCAGAACTG$ GGAGGAGGAGGAGGACGACCACCATCATCACCACGACAACTGTTACCACTACGGTGACCAGCCCAGTTCTG TGTAATAACAACATCTCCGAGGGCGAAGGGTATGTGGAGTCTCCAGATCTGGGGAGCCCCGTCAGCCGCACCCTG CAGGGAGAGGAGACCCTCATCTGCCTCAATGGCACCCGGCCATCCTGGAACGGTGAAACCCCCAGCTGCATGGCA AACCTCACCTGCCGTTGGGTCATTGAAGCAGCTGAGGGGCCCCGGCTGCACCTTCAAAGGGTCTCGCTG GATGAGGACAATGACCGGCTGATGGTGCGCTCAGGGGGCCCCCCTATCCCCCGTGATCTATGATTCGGACATG GACGATGTCCCCGAGCGGGGTCTCATCAGTGACGCCCAGTCCCTCTACGTGGAGCTGCTGTCAGAGACACCTGCC AATCCCCTGCTGTTAAGCCTTCGATTTGAAGCCTTTGAGGAGGATCGCTGCTTCGCCCCCTTCCTGGCACATGGA AATGTCACTACCACGGACCCTGAGTATCGCCCAGGGGCACTGGCAACCTTCTCGTGCCTCCCAGGATATGCCCTG GAGCCCCCTGGGCCCCCCAATGCCATCGAATGTGTGGATCCCACAGAACCCCACTGGAACGACACAGAGCCGGCC TGCAAAGCCATGTGTGGAGGGGAGCTGTCGGAACCAGCTGGCGTGGTCCTCTCTCCCGACTGGCCCCAGAGCTAT AGCCCGGGCCAAGACTGCGTGTGGGGCGTGCACGTCCAGGAAGAGAGCGCATCTTGCTCCAAGTTGAGATATTG AATGTGCGGGAAGGGGACATGCTGACGCTGTTCGACGGGGACGGTCCCAGCGCCCGAGTCTTGGCCCAGCTGCGG GGACCTCAGCCGCCGCCGCCCTTCTCTCTCTGGGCCCGACCTCACACTGCAGTTTCAGGCACCGCCCGGGCCC CCAAATCCAGGCCTGGGCCAGGGCTTCGTATTGCACTTCAAAGAGGTCCCGAGGAACGACACGTGCCCCGAGCTG CCACCTCCGGAGTGGGGCTGGAGAACGGCATCCCACGGGGACCTGATCCGGGGCACGGTGCTCACCTACCAGTGC GAGCCTGGCTACGAGCTGCTAGGCTCCGACATTCTCACTTGCCAGTGGGACCTGTCTTGGAGCGCCGCCGCCCCC GCCTGCCAAAAGATCATGACTTGTGCTGACCCTGGCGAGATTGCCAACGGGCACCGCACCGCCTCGGACGCCGGC TTCCCCGTTGGCTCCCACGTCCAGTACCGCTGCCTGCCAGGGTACAGCCTCGAGGGGGCAGCCATGCTCACCTGC TACAGCCGGGACACGGCACACCCAAGTGGAGCGATAGGGTCCCCAAATGCGCCTTGAAGTACGAGCCGTGCCTG TTCTGCTATGAGGGCTTTGAGCTTATCGGCGAGGTCACCATCACCTGTGTGCCCGGCCACCCCTCCCAGTGGACC AGCCAGCCCCACTCTGCAAAGTGACCCAGACCACAGATCCATCACGGCAGCTGGAAGGGGGGAACCTGGCCCTG GCCATCCTGCTGCCTCTAGGCTTGGTCATTGTCCTCGGCAGTGGCGTTTACATCTACTACACCAAGCTTCAGGGA AAGTCCCTTTTCGGCTTCTCGGGCTCCCACTCCTACAGCCCCATCACCGTGGAGTCGGACTTCAGCAACCCGCTG ${\tt TATGAAGCTGGGGATACGCGGGAGTATGAAGTTTCCATC} \underline{{\tt TGA}}{\tt ACCCCAAGACTACAGCTGCAGGACCCAGGACGC}$ CCGCCCAAAAA

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FIGURE 112

MGTPRAQHPPPPQLLFLILLSCPWIQGLPLKEEEILPEPGSETPTVASEALAELLHGALLRRG
PEMGYLPGSDPDPTLATPPAGQTLAVPSLPRATEPGTGPLTTAVTPNGVRGAGPTAPELLTPP
PGTTAPPPPSPASPGPPLGPEGGEEETTTTIITTTVTTTVTSPVLCNNNISEGEGYVESPDL
GSPVSRTLGLLDCTYSIHVYPGYGIEIQVQTLNLSQEEELLVLAGGGSPGLAPRLLANSSMLG
EGQVLRSPTNRLLLHFQSPRVPRGGGFRIHYQAYLLSCGFPPRPAHGDVSVTDLHPGGTATFH
CDSGYQLQGEETLICLNGTRPSWNGETPSCMASCGGTIHNATLGRIVSPEPGGAVGPNLTCRW
VIEAAEGRRLHLHFERVSLDEDNDRLMVRSGGSPLSPVIYDSDMDDVPERGLISDAQSLYVEL
LSETPANPLLLSLRFEAFEEDRCFAPFLAHGNVTTTDPEYRPGALATFSCLPGYALEPPGPPN
AIECVDPTEPHWNDTEPACKAMCGGELSEPAGVVLSPDWPQSYSPGQDCVWGVHVQEEKRILL
QVEILNVREGDMLTLFDGDGPSARVLAQLRGPQPRRRLLSSGPDLTLQFQAPPGPPNPGLGQG
FVLHFKEVPRNDTCPELPPPEWGWRTASHGDLIRGTVLTYQCEPGYELLGSDILTCQWDLSWS
AAPPACQKIMTCADPGEIANGHRTASDAGFPVGSHVQYRCLPGYSLEGAAMLTCYSRDTGTPK
WSDRVPKCALKYEPCLNPGVPENGYQTLYKHHYQAGESLRFFCYEGFELIGEVTITCVPGHPS
QWTSQPPLCKVTQTTDPSRQLEGGNLALAILLPLGLVIVLGSGVYIYYTKLQGKSLFGFSGSH
SYSPITVESDFSNPLYEAGDTREYEVSI

Important features of the protein:

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 842-864

N-glycosylation sites.

amino acids 176-180, 222-226, 247-251, 332-336, 355-359, 373-377, 473-477, 517-521, 641-645

Tyrosine kinase phosphorylation site.

amino acids 61-69

N-myristoylation sites.

amino acids 2-8, 84-90, 111-117, 114-120, 190-196, 198-204, 235-241, 309-315, 333-339, 351-357, 472-478, 484-490, 528-534, 626-632, 665-671, 775-781, 842-848

Amidation site.

amino acids 384-388

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 12-23

CUB domain proteins profile.

amino acids 202-218, 376-392, 553-569

FIGURE 113

GCCGCGGCGGAGCTGCCTGCCGGTCCCGCGCGCGCGCGCTCCGCACTCCTCGGCCCTCGGGCGGTCGATGGGACGG GGCGCCGCGGAGCAGGAGGCGCCCCGTCGGGGTGCTCGGGCCGCGGGGAGCCCACTGTGGGGCTCGGGCATG GCGGGCCGCAGGACCTGAGCTCTCCTCAGGGGAGCGGGGAGGCAGCTGCTGGCCGGCGATGGGGACGGAGTGGGG CCGTCGCCGCCGCGCGAGCCGTGAGCGCCGAGCCACCGCCGCTACCTCAGCCCTTCGCGAAGCGCCGGGCA GCTCGGGAACATGGCCCTGGAGCGGCTCTGCTCGGTCCTCAAAGTGTTGTTAATAACAGTACTGGTAGTGGAAGG GATTGCCGTGGCCCAAAAAACCCAAGATGGACAAAATATTGGAATCAAGCATATTCCTGCAACCCAGTGTGGCAT TTGGGTTCGAACCAGCAATGGAGGTCATTTTGCTTCGCCAAATTATCCTGACTCATATCCACCAAACAAGGAGTG TATCTACATTTTGGAAGCTGCTCCACGTCAAAGAATAGAGTTGACCTTTGATGAACATTATTATATAGAACCATC ATTTGAGTGTCGGTTTGATCACTTGGAAGTTCGAGATGGGCCATTTGGTTTCTCTCCTCTTATAGATCGTTACTG TGGCGTGAAAAGCCCTCCATTAATTAGATCAACAGGGAGATTCATGTGGATTAAGTTTAGTTCTGATGAAGAGCT TCCCATTCCAGATTGTCAGTTCGAGCTCTCGGGAGCTGATGGAATAGTGCGCTCTAGTCAGGTAGAACAAGAGGA GTTCCTAGATTATCAAATGGAGCACTCAAATGAATGCAAGAGAAACTTCGTTGCAGTCTATGATGGAAGCAGTTC TATTGAAAACCTGAAGGCCAAGTTTTGCAGCACTGTGGCCAATGATGTAATGCTTAAAACAGGAATTGGAGTGAT ${\tt TCGAATGTGGGCAGATGAAGGTAGTCGGCTTAGCAGGTTTCGAATGCTCTTTACTTCCTTTGTGGAGCCTCCCTG}$ CACAAGCAGCACTTTCTTTTGCCATAGCAACATGTGCATCAATAATTCTTTAGTCTGTAATGGTGTCCAAAATTG TGGAACAATTATTGGCATTACTTCAGGGATTGTCTTGGTCCTTCTCATTATTTCTATTTTAGTACAAGTGAAACA GCCTCGAAAAAAGGTCATGGCTTGCAAAACCGCTTTTAATAAAACCGGGTTCCAAGAAGTGTTTGATCCTCCTCA TTATGAACTGTTTTCACTAAGGGACAAAGAGATTTCTGCAGACCTGGCAGACTTGTCGGAAGAATTGGACAACTA $\verb|CCAGAAGATGCGGCGCTCCTCCACCGCTTCCACGACCACCACCTGTGGGTCGCAGGCCTCCAGCGT|\\$ CAAACAAGCAGGACCAACCTCAGTTCCATGGAACTTCCTTTCCGAAATGACTTTGCACAACCACAGCCAATGAA AACATTTAATAGCACCTTCAAGAAAAGTAGTTACACTTTCAAACAGGGACATGAGTGCCCTGAGCAGGCCCTGGA AGACCGAGTAATGGAGGAGATTCCCTGTGAAATTTATGTCAGGGGGCGAGAAGATTCTGCACAAGCATCCATATC ACTGTTTCCAGCAGCCAACCCTTTTCTCCCATCACAACTACGAAGACCTTGATTTACCGTTAACCTATTGTATGG TGATGTTTTTATTCTCTCAGGCAGTCTATATATGTTAAACCAATCAAGGAACTTACTCTATTCAGTGGAAACAAT AATCATCTCTATTGCTTGGTGTCATTTATAGGAAGCACTGCCAGTTAAAGAGCATTAGAAGAGGTGGTTGGATGG AGCCAGGCTCAGGCTGCCTCTTCGTTTTAGCAACAAGAAGACTGCTCTTGACTGATAACAGCTCTGTCAATATTT TGATGCCACAATAAACTTGATTTTTTTTTACATTCCTTTTATTTTTCCTTTCTCTAAATTTAATTTGTTTTATAA GCCTATCGTTTTACCATTTCATTTTCTTACATAAGTACAAGTGGTTAATGTACCACATACTTCAGTATAGGCATT TGTTCTTGAGTGTGTCAAAATACAGCTAGTTACTGTGCCAATTAAGACCCAGTTGTATTTCACCCATCTGTTTCT TCTTGGCTAATCTCTGTACTTCTGCCTTTTAATTACTGGGCCCTTATTCCTTATTTCTGTGAGAAATAATAGAT GATATGATTATTACCTTTCAATTATATTTTTCTCAGTTATACTAGAAAATTTCATAATCCTGGGATATATGTAC CATTGTCAGCTATGACTAAAAATTTGAAAAAGATAAAAATTTCTAGCAAGCCTTTGAAGTTTACCAAGTATAGTC TTTGCAATGTTTCTCTTCGCTAGATTGTTACATAGCTCCCATTCTGTTGGTTTTGCTTACAGCATATGGTAACCA AGGTTAGATGCCAGTTAAAATTCCTTAGAAATTGGATGAGCCTTGAGATTGCTTCTTAACTGGGACATGACATTT CAATAATTTATAAACATAAAAGCTCATTGTGTTTTTTTTAGACTTTTGATATTTTGATACTGTACAAACTTTATT **AAATCAAGATGAAAGACCTACAGGACAGATTCCTTTCAGTGTTCACATCAGTGGCTTTGTATGCAAATATGCTGT** TGTATTTAGTTTGTGATAAATTTTTCACTGTGTGATATTTATGCTCTAAATCACACAAATCCCATATTAAAA TATACATTGTACCTGAAAAAAAA

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FIGURE 114

MALERLCSVLKVLLITVLVVEGIAVAQKTQDGQNIGIKHIPATQCGIWVRTSNGGHFASPNYP
DSYPPNKECIYILEAAPRQRIELTFDEHYYIEPSFECRFDHLEVRDGPFGFSPLIDRYCGVKS
PPLIRSTGRFMWIKFSSDEELEGLGFRAKYSFIPDPDFTYLGGILNPIPDCQFELSGADGIVR
SSQVEQEEKTKPGQAVDCIWTIKATPKAKIYLRFLDYQMEHSNECKRNFVAVYDGSSSIENLK
AKFCSTVANDVMLKTGIGVIRMWADEGSRLSRFRMLFTSFVEPPCTSSTFFCHSNMCINNSLV
CNGVQNCAYPWDENHCKEKKKAGVFEQITKTHGTIIGITSGIVLVLLIISILVQVKQPRKKVM
ACKTAFNKTGFQEVFDPPHYELFSLRDKEISADLADLSEELDNYQKMRRSSTASRCIHDHHCG
SQASSVKQSRTNLSSMELPFRNDFAQPQPMKTFNSTFKKSSYTFKQGHECPEQALEDRVMEEI
PCEIYVRGREDSAQASISIDF

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 348-369

N-glycosylation sites.

amino acids 311-315, 385-389, 453-457, 475-479

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 426-430, 479-483

N-myristoylation sites.

amino acids 22-28, 32-38, 54-60, 186-192, 279-285, 318-324, 348-354, 352-358, 441-447

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FIGURE 115

GGTCTCTGTCCTTGGCTGTGGCTCCTGCGCTCTGGCTGAGCCATC CTCACTGAGCTTGGAAGACTGCAAGCCCACGAAGGTTCTGAAGGAATATTTCTGCATGTCACA GTTCCACGGAAGATTAAGTCAAATGACAGTGAAGTTTCAGAGAGGAAGATGATTTACATCATT ACAATTGATGGACAACCTTACACTCTACATCTCGGAAAACAATCATTCTTACCCCAGAACTTT TTGGTTTATACATATAATGAAACTGGATCTTTGCATTCTGTGTCTCCATATTTTATGATGCAT TGCCATTACCAAGGATATGCTGCCGAATTTCCAAATTCATTTGTGACACTCAGTATATGTTCT GGTCTCAGGGGATTTCTCCAGTTTGAAAATATCAGTTATGGAATTGAACCAGTAGAATCTTCA GCAAGATTTGAGCATATAATTTATCAAATGAAAAAATAATGATCCAAATGTATCCATTTTAGCA GTAAATTACAGTCATATTTGGCAGAAAGACCAGCCCTACAAAGTTCCTTTAAACTCACAGATA AAAAATCTTTCAAAACTATTACCCCAATATCTGGAAATATACATTATAGTGGAAAAAGCTTTG ATGTTTACCCAGTTCAAATTGACTGTTATACTGTCTTCCTTGGAATTGTGGTCAAATGAAAAC CAGATTTCCACCAGTGGGGATGCTGATGATATTACAAAGATTTTTGGCATGGAAACGGGAC TATCTCATCCTACGGCCCCATGACATAGCATACTTACTTGTTTACAGGAAACATCCTAAATAT GTGGGAGCAACATTTCCTGGCACCGTATGCAATAAAAGCTATGATGCAGGTATTGCTATGTAT CCAGATGCAATAGGTTTGGAGGGATTTTCGGTTATTATAGCTCAACTGCTTGGCCTTAATGTA GGATTAACATATGATGACATCACTCAGTGTTTCTGTCTGAGAGCTACATGCATCATGAATCAT GAAGCAGTGAGTGCCAGTGGTAGAAAGATTTTTAGCAACTGCAGCATGCACGACTATAGATAT TTTGTTTCAAAATTTGAGACTAAATGCCTTCAGAAGCTTTCAAATTTGCAACCATTACATCAA AATCAACCAGTGTGTGGTAATGGGATTTTGGAATCCAATGAAGAATGTGACTGTGGTAATAAA AATGAATGTCAATTTAAGAAGTGCTGTGATTATAACACATGTAAACTGAAGGGCTCAGTAAAA TGTGGTTCTGGACCATGTTGTACATCAAAGTGTGAGTTGTCAATAGCAGGCACTCCATGTAGA AAGAGTATTGATCCAGAGTGTGATTTTACAGAGTACTGCAATGGAACCTCTAGTAATTGTGTT CCTGACACTTATGCACTGAATGGCCGTTTGTGCAAGTTGGGAACTGCCTATTGCTATAACGGA CAATGTCAAACTACTGATAACCAGTGTGCCAAGATATTTGGAAAAGGTGCTCAAGGTGCTCCA TTTGCCTGTTTTAAAGAAGTTAATTCTCTGCATGAAAGATCTGAAAACTGTGGTTTTAAAAAT TCACAACCATTACCTTGTGAACGGAAGGATGTTCTCTGTGGAAAATTAGCTTGTGTTCAGCCA CATAAAAATGCTAATAAAAGTGACGCTCAATCTACAGTTTATTCATATATTCAAGACCATGTA TGTGTATCTATAGCCACTGGTTCCTCCATGAGATCAGATGGAACAGACAATGCCTATGTGGCT ATGGGATATAACTGTAATGCCACCACAAAATGCAAAGGGAAAGGGATATGTAATAATTTTGGT AATTGTCAATGCTTCCCTGGACATAGACCTCCAGATTGTAAATTCCAGTTTGGTTCCCCAGGG GGTAGTATTGATGATGGAAATTTTCAGAAATCTGGTGACTTTTATACTGAAAAAGGCTACAAT ACACACTGGAACAACTGGTTTATTCTGAGTTTCTGCATTTTTCTGCCGTTTTTCATAGTTTTC ACCACTGTGATCTTTAAAAGAAATGAAATAAGTAAATCATGTAACAGAGAGAATGCAGAGTAT AATCGTAATTCATCCGTTGTATCAGAAAGCGATGACGTGGGACAT<u>TAA</u>TATTGCACAGAACTT ATTGTAAATGTCAAACTTTTGGAAAATAAAGCCTGCGTGCCCTCCC

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FIGURE 116

MFLLALTELGRLQAHEGSEGIFLHVTVPRKIKSNDSEVSERKMIYIITIDGQPYTLHLGKQ
SFLPQNFLVYTYNETGSLHSVSPYFMMHCHYQGYAAEFPNSFVTLSICSGLRGFLQFENISYG
IEPVESSARFEHIIYQMKNNDPNVSILAVNYSHIWQKDQPYKVPLNSQIKNLSKLLPQYLEIY
IIVEKALMFTQFKLTVILSSLELWSNENQISTSGDADDILQRFLAWKRDYLILRPHDIAYLLV
YRKHPKYVGATFPGTVCNKSYDAGIAMYPDAIGLEGFSVIIAQLLGLNVGLTYDDITQCFCLR
ATCIMNHEAVSASGRKIFSNCSMHDYRYFVSKFETKCLQKLSNLQPLHQNQPVCGNGILESNE
ECDCGNKNECQFKKCCDYNTCKLKGSVKCGSGPCCTSKCELSIAGTPCRKSIDPECDFTEYCN
GTSSNCVPDTYALNGRLCKLGTAYCYNGQCQTTDNQCAKIFGKGAQGAPFACFKEVNSLHERS
ENCGFKNSQPLPCERKDVLCGKLACVQPHKNANKSDAQSTVYSYIQDHVCVSIATGSSMRSDG
TDNAYVADGTMCGPEMYCVNKTCRKVHLMGYNCNATTKCKGKGICNNFGNCQCFPGHRPPDCK
FQFGSPGGSIDDGNFQKSGDFYTEKGYNTHWNNWFILSFCIFLPFFIVFTTVIFKRNEISKSC
NRENAEYNRNSSVVSESDDVGH

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 665-684

N-glycosylation sites.

amino acids 36-39, 76-79, 122-125, 149-152, 156-159, 177-180, 270-273, 335-338, 441-444, 537-540, 587-590, 601-604, 703-706

Casein kinase II phosphorylation sites.

amino acids 74-77, 208-211, 221-224, 304-307, 337-340, 346-349, 376-380, 415-418, 499-502, 639-642, 708-711

Tyrosine kinase phosphorylation site.

amino acids 243-249

N-myristoylation sites.

amino acids 53-58, 79-84, 266-271, 298-303, 372-377, 403-408, 408-413, 442-447, 462-467, 469-474, 488-493, 567-572, 610-615, 616-621, 634-639

Amidation site.

amino acids 328-331

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FIGURE 117

CCCACGCGTCCGCGGACGCGTGGGGCTCAGTGGGCGTCGCGCGAAGGCTAAGGGAGTGTGGCG GGCGGCTCCGGGAGCCAACATGCCTCGGTATGCGCAGCTGGTCATGGGCCCCGCGGGCAGCGG GAAGAGCACCTACTGTGCCACCATGGTCCAGCACTGTGAAGCCCTCAACCGGTCTGTCCAAGT TGTAAACCTGGATCCAGCAGCAGAACACTTCAACTACTCCGTGATGGCTGACATCCGGGAACT GATCGAGGTGGATGATGTAATGGAGGATGATTCTCTGCGATTCGGTCCCAACGGAGGATTGGT GAAACATCTGGTCCAGCAGCTCGAGCAGTGGGAGTTCCGAGTCTGTGGAGTTTTTCTTGTTGA TTCTCAGTTCATGGTGGAGTCATTCAAGTTTATTTCTGGCATCTTGGCAGCCCTGAGTGCCAT GATCTCTCTAGAAATTCCGCAAGTCAACATCATGACAAAAATGGATCTGCTGAGTAAAAAAGC AAAAAGGAAATTGAGAAATTTTTAGATCCAGACATGTATTCTTTATTAGAAGATTCTACAAG CAGCATGGTTCGATTTTTACCTTACGATCAGTCAGATGAAGAAAGCATGAACATTGTATTGCA GCATATTGATTTTGCCATTCAATATGGAGAAGACCTAGAATTTAAAGAACCAAAGGAACGTGA AGATGAGTCTTCCTCTATGTTTGACGAATATTTTCAAGAATGCCAGGATGAA**TGA**AGAGTTTA CTAAAAGTAACCATCTAAAGAGCTTGTGGCCAAACCAGCAGAACATTCTTCTCTCTAAAGGAT GCAATAGTAGAAAGCTACTTATTTAATGAAAAAAGTAAAACTTCGTTCTTTATCAGCCTCA TGCCTGAATCAAATTTTTAATTATTCTGAAACTGCTGCTGTTTAAAGTGGAATCTTTTAGTAT TAAATTAGCACCTGAGCTAAGGTTAAGGCCGGTCTAAACTTATTTTCACTTTTTGTATTATTT TTGAGATGCAGGAATTACTGTAACAAAATATGTATGTCCGAAGGGAAAAAGCTGCAAGGATAT ATAACTTAAAAAGTAAAAATAACTATGTTTTGAGAT

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FIGURE 118

MPRYAQLVMGPAGSGKSTYCATMVQHCEALNRSVQVVNLDPAAEHFNYSVMADIRELIEVDDV
MEDDSLRFGPNGGLVFCMEYFANNFDWLENCLGHVEDDYILFDCPGQIELYTHLPVMKHLVQQ
LEQWEFRVCGVFLVDSQFMVESFKFISGILAALSAMISLEIPQVNIMTKMDLLSKKAKKEIEK
FLDPDMYSLLEDSTSDLRSKKFKKLTKAICGLIDDYSMVRFLPYDQSDEESMNIVLQHIDFAI
OYGEDLEFKEPKEREDESSSMFDEYFQECQDE

Important features of the protein:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 151-170

N-glycosylation sites.

amino acids 31-35, 47-51

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 212-216

Tyrosine kinase phosphorylation site.

amino acids 189-197

N-myristoylation sites.

amino acids 13-19, 76-82, 154-160

ATP/GTP-binding site motif A (P-loop).

amino acids 10-18

FIGURE 119

GGGCGCTGGGAGACACCGGACGCCCGCTCGGCTGCGCTGCGGCTCAGGCCCCCGCTCGGGCCC GACCCGCTCGGTCACCGCCGGCTCGGGCCGCCACCTGCCGGCTGCGGCCCCAGGGCCATGCGG AGGCCCACGAGGGGGCCGCGCCACGCGCATCCCGTAGCCCAGGTGGCCCAGGTCTGCACCG CGGCGGCCTCGGCGCCATGGAGCCCCCGTATTCGCTGACGCGCACTACGATGAGTTCCAAGA GGTCAAGTACGTGAGCCGCTGCGGCGGGGGGGGGCGCGGGGGCCTCCCTGCCCCCGGGCTT CCCGTTGGGCGCTGCGCGCGCTCACCGGGGCCCGGTCCGGGCTGCCGCGCTGGAACCGGCG CGAGGTGTGCCTGCTGTCGGGGCTGGTGTTCGCCGCCGGCCTCTGCGCCATTCTGGCGGCTAT GCTGGCCCTCAAGTACCTGGGCCCGGTCGCGGCCGGCGGCGCGCCTGTCCCGAGGGCTGCCC TGAGCGCAAGGCCTTCGCGCGCGCCGCTCGCTTCCTGGCCGCCAACCTGGACGCCAGCATCGA CCCATGCCAGGACTTCTACTCGTTCGCCTGCGGCGGTTGGCTGCGGCGCCACGCCATCCCCGA CGACAAGCTCACCTATGGCACCATCGCGGCCATCGGCGAGCAAAACGAGGAGCGCCTACGGCG CCTGCTGGCGCGCCCGGGGGTGGGCCTGGCGCGCGCCCAGCGCAAGGTGCGCCCTTCTT CCGCTCGTGCCTCGACATGCGCGAGATCGAGCGACTGGGCCCGCGACCCATGCTAGAGGTCAT CGAGGACTGCGGGGGCTGGGACCTGGGCGGCGCGGAGGAGCGTCCGGGGGTCGCGGCGATG GGACCTCAACCGGCTGCTGTACAAGGCGCAGGGCGTGTACAGCGCCGCCGCCTCTTCTCGCT CACGGTCAGCCTGGACGACAGGAACTCCTCGCGCTACGTCATCCGCATTGACCAGGATGGGCT CACCCTGCCAGAGAGGACCCTGTACCTCGCTCAGGATGAGGACAGTGAGAAGATCCTGGCAGC ATACAGGGTGTTCATGGAGCGAGTGCTCAGCCTCCTGGGTGCAGACGCTGTGGAACAGAAGGC CCAAGAGATCCTGCAAGTGGAGCAGCAGCTGGCCAACATCACTGTGTCAGAGTATGACGACCT ACGGCGAGATGTCAGCTCCATGTACAACAAGGTGACGCTGGGGCAGCTGCAGAAGATCACCCC CCACTTGCGGTGGAAGTGGCTGCTAGACCAGATCTTCCAGGAGGACTTCTCAGAGGAAGAGGA GGTGGTGCTGCCGACAGACTACATGCAGCAGGTGTCGCAGCTCATCCGCTCCACACCCCA CCGGGTCCTGCACAACTACCTGGTGTGGCGCGTGGTGGTGGTCCTGAGTGAACACCTGTCCCC GCCATTCCGTGAGGCACTGCACGAGCTGGCACAGGAGATGGAGGGCAGCGACAAGCCACAGGA GCTGGCCCGGGTCTGCTTGGGCCAGGCCAATCGCCACTTTGGCATGGCGCTTTGGCGCCCTCTT TGTACATGAGCACTTCTCAGCCGCCAGCAAAGCCAAGGTGCAGCAGCTAGTGGAAGACATCAA TCGGGCCAAGCTCCAGTACATGATGGTGATGGTCGGCTACCCGGACTTCCTGCTGAAACCCGA TGCTGTGGACAAGGAGTATGAGTTTGAGGTCCATGAGAAGACCTACTTCAAGAACATCTTGAA CAGCATCCCCTTCAGCATCCAGCTCTCAGTTAAGAAGATTCGGCAGGAGGTGGACAAGTCCAC GTGGCTGCTCCCCCACAGGCGCTCAATGCCTACTATCTACCCAACAAGAACCAGATGGTGTT CCCCGCGGGCATCCTGCAGCCCACCCTGTACGACCCTGACTTCCCACAGTCTCTCAACTACGG GGGCATCGCCATCATTGGACATGAGCTGACCCACGGCTACGACGACTGGGGGGGCCCAGTA TGACCGCTCAGGGAACCTGCTGCACTGGTGGACGGAGGCCTCCTACAGCCGCTTCCTGCGAAA GGCTGAGTGCATCGTCCGTCTCTATGACAACTTCACTGTCTACAACCAGCGGGTGAACGGGAA ACACACGCTTGGGGAGAACATCGCAGATATGGGCGTCCTCAAGCTGGCCTACCACGCCTATCA GAAGTGGGTGCGGGAGCACGGCCCAGAGCACCCACTTCCCCGGCTCAAGTACACACATGACCA GCTCTTCTTCATTGCCCTTTGCCCAGAACTGGTGCATCAAGCGGCGGTCGCAGTCCATCTACCT GCAGGTGCTGACTGACAAGCATGCCCCTGAGCACTACAGGGTGCTGGGCAGTGTCCCCAGTT TGAGGAGTTTGGCCGGGCTTTCCACTGTCCCAAGGACTCACCCATGAACCCTGCCCACAAGTG $\verb|TTCCGTGTGG| \hline \textbf{TGA} \\ \texttt{GCCTGCCTGCCCCGCCTGCACGCCCCCACTGCCCCGCACGAATCACCTCC}$ TGCTGGCTACCGGGGCAGGCATGCACCCGGTGCCAGCCCCGCTCTGGGCACCACCTGCCTTCC AGCCCTCCAGGACCCGGTCCCCTGCTGCCCCTCACTTCAGGAGGGGCCTGGAGCAGGGTGA GGCTGGACTTTGGGGGGCTGTGAGGGAAATATACTGGGGTCCCCAGATTCTGCTCTAAGGGGG CCAGACCCTCTGCCAGGCTGGATTGTACGGGCCCCACCTTCGCTGTTCTTGCTGCAAAGTC TGGTCAATAAATCACTGCACTGTTAAAAAAAAA

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FIGURE 120

MEPPYSLTAHYDEFQEVKYVSRCGAGGARGASLPPGFPLGAARSVTGARSGLPRWNRREVCLL
SGLVFAAGLCAILAAMLALKYLGPVAAGGGACPEGCPERKAFARAARFLAANLDASIDPCQDF
YSFACGGWLRRHAIPDDKLTYGTIAAIGEQNEERLRRLLARPGGGPGGAAQRKVRAFFRSCLD
MREIERLGPRPMLEVIEDCGGWDLGGAEERPGVAARWDLNRLLYKAQGVYSAAALFSLTVSLD
DRNSSRYVIRIDQDGLTLPERTLYLAQDEDSEKILAAYRVFMERVLSLLGADAVEQKAQEILQ
VEQQLANITVSEYDDLRRDVSSMYNKVTLGQLQKITPHLRWKWLLDQIFQEDFSEEEEVVLLA
TDYMQQVSQLIRSTPHRVLHNYLVWRVVVVLSEHLSPPFREALHELAQEMEGSDKPQELARVC
LGQANRHFGMALGALFVHEHFSAASKAKVQQLVEDIKYILGQRLEELDWMDAETRAAARAKLQ
YMMVMVGYPDFLLKPDAVDKEYEFEVHEKTYFKNILNSIPFSIQLSVKKIRQEVDKSTWLLPP
QALNAYYLPNKNQMVFPAGILQPTLYDPDFPQSLNYGGIGTIIGHELTHGYDDWGGQYDRSGN
LLHWWTEASYSRFLRKAECIVRLYDNFTVYNQRVNGKHTLGENIADMGVLKLAYHAYQKWVRE
HGPEHPLPRLKYTHDQLFFIAFAQNWCIKRRSQSIYLQVLTDKHAPEHYRVLGSVSQFEEFGR
AFHCPKDSPMNPAHKCSVW

Important features of the protein:

Transmembrane domain:

amino acids 64-88

N-glycosylation sites.

amino acids 255-259, 322-326, 656-660

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 722-726

N-myristoylation site.

amino acids 24-30, 26-32, 27-33, 40-46, 47-53, 65-71, 148-154, 169-175, 170-176, 237-243, 450-456, 604-610, 607-613

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 85-96

Prenyl group binding site.

amino acids 772-777

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 609-619

Neutral zinc metallopeptidases, zinc-binding region proteins.

amino acids 609-619

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FIGURE 121

CGGACTGCCGGACCGCGCGTCGACTCGACCGCCAGCGTCGGGGAGGCCCCGGGCGGACCCC AGCGCTGCTTCGGTGGCGTGGTGGAGGTGGGCGCGCACTGGATCCATGGGCCCTCCCGGGGTA ACCCCGTCTTCCAGCTGGCTGCTGAGTACGGGCTGCTGGGGGAGAAGGAGCTGTCCCAGGAGA ACCAGCTGGTGGAGACCGGGGGTCACGTGGGCCTGCCCTCCGTGAGCTACGCCAGCTCCGGGG CCAGCGTGAGCCTCCAGCTGGTGGCGGAGATGGCGACTCTGTTCTACGGCCTGATAGACCAGA CCCGGGAGTTCCTGCACGCTGCAGAGACCCCGGTGCCCAGCGTCGGGGAGTACCTCAAGAAGG AGATTGGCCAGCACGTGGCCGGCTGGACAGAGGATGAGGAGACCAGGAAGCTGAAGCTGGCCG TCCTGAACTCCTTCTTCAACCTGGAATGCTGTGTGAGCGGCACCCACAGCATGGACCTGGTGG CCCTGGCACCCTTTGGGGAGTATACCGTGCTGCCGGGGCTGGACTGCACCTTTTCTAAGGGCT ATCAAGGACTCACAAACTGCATGATGGCCGCCCTGCCGGAGGACACTGTAGTTTTTTGAGAAGC CTGTGAAGACCATCCACTGGAACGGGTCCTTCCAGGAGGCAGCCTTTCCCGGGGAGACCTTTC CAGTGTCGGTAGAGTGTGAGGATGGAGACCGGTTCCCGGCGCACCATGTCATCGTCACCGTGC CAGAAGCAATCAGGAAGATAGGCTTTGGGACCAACAACAAAATCTTCCTGGAGTTTGAGGAGC CCTTCTGGGAGCCAGACTGCCAGCTGATCCAGCTGGTGTGGGAGGACACGTCGCCCCTGGAGG CCTTTGCGTCTGTCCACGTTCTCTGTGGGTTCATTGCCGGACTTGAGTCTGAGTTCATGGAGA CTCTGTCGGATGAAGAAGTACTTCTGTGTCTCACCCAAGTGCTCCGGAGAGTGACAGGAAACC CACGGCTCCCGCGCCCAAGAGCGTCCTGCGGTCTCGCTGCACAGCGCCCCGTACACTAGGG GGTCCTACAGCTACGTGGCCGTGGGCAGTACTGGGGGGCGACCTGGACCTGCTGGCTCAGCCCC TCCCTGCAGACGCCCCGCCCCCAGCTCCAGATCCTGTTTGCGGGGGAAGCCACACATCGCA CGTTTTACTCCACGACGCACGGGGCTCTGCTGTCGGGATGGAGGGGAGGCCGACCGCCTCCTCA GTCTGTGGGCCCCGCAGGTGCAGCAGCCCAGGCCGAGGCTCTAGCTGGGCCCAGCCTACTCTG TTCCACCCGTGTCGGGGGTAGGCTGGGACCGTCATTTCTTCTGACAGATTTCAGTCTGGCTTG **AAATTTGGGGATGTTAATGAGGGTCCTCTGGTTTTTGGTAACCAGGGCCACCTTCTCAGTTCT** TGTGTCTGTTATTGGAGTCTGGCCAGGGTTGACTTGAGCTGAGACACCAGATGCTCACGGAGA

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FIGURE 122

MESTGSVGEAPGGPRVLVVGGGIAGLGAAQRLCGHSAFPHLRVLEATARAGGRIRSERCFGGV VEVGAHWIHGPSRGNPVFQLAAEYGLLGEKELSQENQLVETGGHVGLPSVSYASSGASVSLQL VAEMATLFYGLIDQTREFLHAAETPVPSVGEYLKKEIGQHVAGWTEDEETRKLKLAVLNSFFN LECCVSGTHSMDLVALAPFGEYTVLPGLDCTFSKGYQGLTNCMMAALPEDTVVFEKPVKTIHW NGSFQEAAFPGETFPVSVECEDGDRFPAHHVIVTVPLGFLREHLDTFFDPPLPAEKAEAIRKI GFGTNNKIFLEFEEPFWEPDCQLIQLVWEDTSPLEDAAPELQDAWFRKLIGFVVLPAFASVHV LCGFIAGLESEFMETLSDEEVLLCLTQVLRRVTGNPRLPAPKSVLRSRWHSAPYTRGSYSYVA VGSTGGDLDLLAQPLPADGAGAQLQILFAGEATHRTFYSTTHGALLSGWREADRLLSLWAPQV OOPRPRL

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 364-385

N-glycosylation site.

amino acids 253-257

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 408-412

N-myristoylation sites.

amino acids 20-26, 21-27, 25-31, 105-111, 119-125, 164-170, 216-222, 227-233, 443-449, 484-490

Aminooxidase Flavin containing amine oxidase:

amino acids 23-497

FIGURE 123

CGGACGCGTGGGGGAAGATGGATAAATAATTCTGTCACACGTGCCCTGGCCTCTGGAGCTCAGCTĞCCAGTCCAC ${\tt GTCTAGGGAATCTTAGCATCTGGGACCAAGACACTTTACAGCAATCATCACCCTTTGCAGAGGAGGTGAGCTCAC}$ TCTCTCAGTCTCCCCGGACTCCTTGAAGCCAGTATCGCTGACCAGCAGTCTTGTCTTCCTCATGCACCTCCTCCT $\verb|CCTTCAGCCTGGGGAGCCGAGCTCAGAGGTCAAGGTGCTAGGCCCTGAGTATCCCATCCTGGCCCTCGTCGGGGAAGGTCAAGGTCAGGCCCTGAGTATCCCATCCTGGCCCTCGTCGGGGAAGGTCA$ GGAGGTGGAGTTCCCGTGCCACCTATGGCCACAGCTGGATGCCCAGCAAATGGAGATCCGCTGGTTCCGGAGTCA GACCAAGTTGGTCAAGGACGACATCGCCTATGGCAGCGTGGTCCTGCAGCTTCACAGCATCATCCCCTCTGACAA GGGCACATATGGCTGCCGCTTCCACTCCGACAACTTCTCTGGCGAAGCTCTCTGGGAACTGGAGGTAGCAGGGCT GGATGCCCAGGACCTGTTCAGTCTGGAAACATCTGTGGTTGTCCGAGCGGGAGCCCTCAGCAATGTGTCCGTCTC CATCCAGAATCTCCTCTTGAGCCAGAAGAAGAGTTGGTGGTCCAGATAGCAGACGTGTTCGTACCCGGAGCCTC GAAGCAGCGGAGAAAGCCGAGAAAAGCTGAGGAAGCAGGCGGAGAAGAGACAAGAGAAACTCACTGCAGAGCTGGA AAAGCTTCAGACAGAGCTTGACTGGAGACGGGCTGAAGGCCAGGCTGAGTGGAGAGCAGCCCAAAAATATGCAGT GGATGTGACGCTGGACCCGGCCTCGGCGCACCCCAGCCTGGAGGTGTCGGAGGATGGCAAGAGCGTGTCTTCCCG CGGGGCGCCGCCAGGCCCCTGGCCACCCGCAGCGGTTCTCGGAGCAGACGTGCGCGCTGAGCCTGGAGCG GTTCTCCGCCGCCGCCACTACTGGGAGGTGCACGTGGGCCGCCGCAGCCGCTGGTTCCTGGGCGCCTGCTGGC GGACTACGAGGCCGGAGAGCTGTCCTTCTTCAACGTGTCCGACGCCTCCCACATCTTCACCTTCCACGACACCCTT $\tt CTCGGGCGCGCTCTGTGCGTACTTCAGGCCCAGGGCCCACGACGCGGCGAACATCCGGATCCCCTGACCATCTG$ $\verb|CCCGCTGCCGGTTAGAGGGACGGGCGTCCCCGAAGAGAACGACAGTGACACCTGGCTACAGCCCTATGAGCCCGC|\\$ GGACCCCGCCTGGACTGGTGGTGAGGCGCCCTCGTGGCCGCGGGACTGGCCCCGGGGGGCCCCCTGGATCCCAG GCCAGCGCTTTGCTCTCCTGCTCCGTCTGAAGGGAGCAGGTGCACCAGCCAAAATGTCAGCGAGGGGGACAAAGA GAGGGACCTTTGCCTACGTAGATGTGTATGTGTAGTGCGATTTTCTTCAAGGAAAGGAGACAAGTCCAAAGCTCG TTTGTGGATTGTGGGACTGAGCGAAGGAGTACAAATATATCCACGTCGCTCAGAGCTGGGGTGCTCACGGTGGGC GGTGGCCAAGAAGCCAGCATGGAAGAAGAAGGGAGAAAACTTTGGTGACTGCCTTAGAGGGGATCAGTTAATTTG TATAGTTTTATATTTTTGTATATGTTTGCTAGCTCTAAAAAGGTCGAGATGCAATAACACTTCGTAAGCAACGA GTTCACCTAAGTAAGGCTCAGATCCTAGTTTTAAAAACCATTTCCCATTAAAATGAAGTTGGAGGAACAGCTGCT GACGGCAACCCGGCAAAAGGGTAGGGAGCCAGGCCGAAGGGGGCCTCACTGACCAATTGTGGGACAATTTGAACAT CAGGATGAATAATGACAGGAGAGATTATAACACACTGAATAAAAACATAATCCATGAGTTCATGCTGATACTCAA ATTTCTTTTTAAAAAGGAGAAACAGGAAGGTTTCTTTTGGAGGTGAAATCTAATTATTGGTGAGAGTCTTGGAGA ACAGGCTGTTTCCAGTCTCAAAGCAGTAACCTTATACACTACTTATAAGTTTGAAAGGGGAAAGGTTACCTTTAC AATGGAGACATCTACCAGATCATCCAAGTGATTAAATTTAACATCATCAATGATGGGACCAAGGACATTATTAGT TTGACAACTGGGGAAAGAAGTGTTCTTCACCCCCTACCCCCAAGACATTCTCTCTGTCGGCCAGGCTGGAGTGCA AGACGGGGGTCTCACTTTGTTACCCAGGCTGGTCTCAAACTCCTGCGCTCAAGCAATCCTCCCACCTGGGCCTCC CAAAATGCTGGGTGTACAGGCATGAGCCGCTGTGCCTGGCTTCATTTTCAGAGTGAGACATTTGTACTGTGGCTA ATGACAACACTTGGTGACTCTAGGTGACTGGTCGACAGATGTTCATTGTACTATCAATGTGGCTTTGCTGTGGGT TTGAAATTTTGCAAACTAAGAGTTGGGTGGCGGGGAGAAGGATACACCAAAAAACTAAGTGATTATCTTTGGATG GGAAAATGTTTGGTAATTGCATTCTTAAAATGTCTTCTTTGTATTTTTTAATGTTCAATAATGTATATGTATCAG TTCTGTAATAAAGGGGAAAACACTTTTCA

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FIGURE 124

MVDLSVSPDSLKPVSLTSSLVFLMHLLLLQPGEPSSEVKVLGPEYPILALVGEEVEFPCHLWP
QLDAQQMEIRWFRSQTFNVVHLYQEQQELPGRQMPAFRNRTKLVKDDIAYGSVVLQLHSIIPS
DKGTYGCRFHSDNFSGEALWELEVAGLGSDPHLSLEGFKEGGIQLRLRSSGWYPKPKVQWRDH
QGQCLPPEFEAIVWDAQDLFSLETSVVVRAGALSNVSVSIQNLLLSQKKELVVQIADVFVPGA
SAWKSAFVATLPLLLVLAALALGVLRKQRRSREKLRKQAEKRQEKLTAELEKLQTELDWRRAE
GQAEWRAAQKYAVDVTLDPASAHPSLEVSEDGKSVSSRGAPPGPAPGHPQRFSEQTCALSLER
FSAGRHYWEVHVGRRSRWFLGACLAAVPRAGPARLSPAAGYWVLGLWNGCEYFVLAPHRVALT
LRVPPRRLGVFLDYEAGELSFFNVSDGSHIFTFHDTFSGALCAYFRPRAHDGGEHPDPLTICP
LPVRGTGVPEENDSDTWLQPYEPADPALDWW

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 247-272

N-glycosylation sites.

amino acids 102-106, 139-143, 224-228, 464-468, 516-520

Tyrosine kinase phosphorylation site.

amino acids 105-114

N-myristoylation sites.

amino acids 129-135, 220-226, 399-405, 423-429, 480-486

Amidation site.

amino acids 390-394

FIGURE 125

TATAGTCCCAGCTACTCATGGGGCTGATGCAGGTTGAGGCAGGAGGTTCATGAGCCCAGGAGGTTGGAGCTGTAA ACCAATGCTGCAGGAAAAAGCAACATATTTAAGTTATCCAATAACACCTATCCAATAATTGTAAATCATTATCAT GACATGGTAGAGTTGTTTATATTTCTTTTCCTTTTAGGTGAAACACCATTCAAAGTCGTAGTCAAATCTCTTTCA CCTAAAGAGTTGGTCCGGATACATGTCCCTAAACCTTTGGACAGGAATGATGGAACATTTTTGATGAGATATAGG ATGTATGAAACTGTCGATGAAGGCCTGAAGATAGAGGTCCTTTATGGTGATGAACATGTGGCTCAGTCTCCCTAT ATTTTGAAAGGACCAGTGTACCATGAGTACTGTGAGTGTCCGGAAGATCCTCAGGCCTGGCAGAAGACTCTTTCT TGTCCAACCAAGGAACCACAGATTGCAAAAGATTTTGCTTCCTTTCCCAGCATCAATCTCCAGCAAATGCTAAAA GAAGTCCCCAAAAGGTTTGGGGATGAGAGAGGTGCCATTGTTCATTACACGATTCTCAATAACCATGTTTACCGG AGATCTTTAGGGAAATACACAGACTTCAAGATGTTCTCTGATGAGATTTTTGTTATCATTGACAAGAAAGGTCCTT CTCCCAGATTTAGAATTTTATGTTAATCTTGGAGATTGGCCCTTGGAGCATCGAAAAGTCAATGGAACCCCTAGC CCCATACCTATCATTTCATGGTGTGGCTCTCTGGATTCAAGAGATGTTGTCCTTCCAACGTATGACATCACCCAC TCCATGCTTGAAGCCATGCGGGGTGTTACAAATGATCTCCTCTCTATTCAGGGAAATACAGGGCCTTCCTGGATC AATAAAACAGAGAGGCTTTCTTCAGAGGTAGAGACAGCCGAGAGGGGGGCTCCAGTTGGTACAGCTGTCCAAA GAAAATCCTCAGCTACTAGATGCAGGAATTACAGGATATTTCTTTTTCCAAGAGAAAAGGAAAAGGAGCTTGGAAAA GCCAAGTTGATGGGTTTCTTTGATTTCTTTAAGTACAAGTATCAAGTAAATGTGGATGGGACCGTGGCTGCTTAC AGATATCCATATCTCATGCTGGGCGACAGTCTGGTTTTAAAGCAGGACTCGCCATATTATGAACATTTCTACATG GCACTAGAACCTTGGAAGCATTATGTTCCAATTAAAAGAAATCTGAGTGATTTATTAGAGAAAGTTAAATGGGCT AAGGAAAATGATGAAGAAGCCAAGAAGATTGCAAAAGAAGGACAGTTGATGGCTAGGGACCTACTACAGCCACAC AGGCTTTACTGCTACTATTACCAAGTACTGCAGAAATATGCCGAGCGCCAGTCCAGCAAACCCGAAGTACGTGAT GGAATGGAACTTGTTCCTCAGCCAGAAGATAGCACAGCCATCTGCCAGTGCCACAGGAAAAAGCCTTCAAGAGAA ${\tt GAACTT} \underline{{\tt TGA}} {\tt GTCAGCCCAGAATCACACTCCTGTGTATCCCGGCTACACTTTAAGGAAAGATTGAATCTAAGCTGT$ GAAGGACAGTATAGAAGACTGCACCAAGTGGACTAGTTCTCCCGGTGGCTTTATATATGTAGATGGATATAGCAG TACTGGTTGAGTATCCCTCATCTGAAATGCTTAGGACCAGGAGTGTTTCAGGCTTCAGATTTTTTAAGATTTTGGG **AATATTTGCATGTACATAATGAGGTATCTTGGGGATGAGATCCAAGTCTAAACACAAAATTCATTTATATTTTAT** ATATACCTTGTTCACATACCCTGAAGGTAATTTTATATAATATTTTTAATAATTTGTGCATGAAACAAAGTTTGT ATACATTGAACTGTCAGAAAGCAAAGGTGTCACTATCTTAGCGACCCAAGTGGTGGTGTCAGCACTCAAAAAGTT TTGGATTTTGGGGTATTTCAGATTTTAGATTTTTGTATGAGGAATGTTCAACCTGTATTTGAACAAGCATTACCA AATATCATTGAATATTAATATCTTTTGCGTAAAAACTGCTATTATCAGCATCATAGTTTCTCTAAAAAGAAAACT TTACATATTTTATTGGTTTATTCTATCCCCTGTTCACTTTTTCTCTTCCACTTCCAATTATGAAGAGAAAATAT TTGTTCAGGGTTGTCCCCCCGCCCCCGTCACTGCATAATTTCTCCTCTTACAAGCTGCTTTTGGCTTTCATTAA TAACAGCTTCCTTTTAGAAGGTCTGATAAGGATATTTAAGGAAGAAGAAGAATGACTCTGTTATTAAAGGTGGCAT GGAGACTGTGGAGGGAATATTTTTTAAAGCACTACTCATATCCTTTAAACTAAATTTTGCCAAAGCCCGAGACAA TCAGGTGAAAGGCATTCATCATTTTTAAGCTGAAAAGGGGATCCTTGAAAACACTGAAAACCTCTACAACAATCT TCAGGAAGCCTGCTATCTTGGGATTCACTAATAATAGGCCAAGAACAAAGGCAAGCATCCATTCCTCACTCCACC ACTTTTCTATTTCAGTGGGTGTCATTGCTACGATGAAGACTTTGGAAATTTCCTTTTCTCTTTTAGGACAGGGTCA GGATTTAGGACTCATAGCCTGAAAGCTCATTACATACTCCTTGTAACCATCAGTCCAAGGTTCAGTTCACTAAAG TGCATGTTCTAAAACAAGAGCTATCCTCATTCCAAATTTTAAAATATGTACTCTGGCCGGTTGCAGTGGCTCACG CCTGTAATCCCAGCACTTTGGCAGGCCGAGATGGGCGGATCTTTTGAGGTCAGGAGTTTGAGACCAGCCTGGCCA ACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCAGGCATGGTGGCATTTGCCTGTAATCCCAGCT ACTCGGGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGCAGAGGTTGCAGTGAGCTGAGATTACACCACTG CACTCCAGCCTGGGTGACAGAGTGAGACTCCATCTCAAAAACTGAAAATAAAAATAAAATATGTATTCTCCTAA CTGAAATATTTACTTAATCTGGAAAACAATGTAACTATTTTTAAAGTGGTTACATCTATTCTTGCTGAAGAACAA TAAACAGAATTTTTTGACTAAGCATAACCAAATTTCAGAACAGTCTAATCAATGCCAAGTATCCAAGGCAAACTC TAATACCCATCCATTGTGCAAAACCACAGCACGCAAGTATTAAATAAGAGCAAGCTGTCCTGAGCCCATACCTA ATGAATTTGTGTCTTAAATATTGTACATTGTGTTTGAGGCTTGTCAAAACTGGGATTATGGCAAGAAAGGTTGCC TAACTCATACCTTTCTGCCTCAAATTCCAGGTGCTAAAGGCTAATGGCATTTTAAACATCTTACATTTTTAAAAA TTTATATTGCCTCTGCCAAACAGGCCTAATAGTTAAAAGCAAGTTGAGACAAACCAGGCAGATTCAGTGTGTGGA ACAGGAAGGATGTGCTTTAAAAAAAGGTGGAATCCCTCAAAAAATTCTATAGGGAGACAGCCGTTAATCTACA TAATTCTTCATCTCGCCAATTCAGCCGCAGCCTTTAAAGAGTTAGTGTTAATGGCTTTCTGGTTTGAAAACAAAA ATGCATCTATGTGGTTGAAAGTTTGGGAGGAGATTCACCAATATCTGAGGAGAAGATGGAGTGAAGGGAATTCTT AAAAATGCCAACCTTAGAAAAGACAATAAATGCACAAAAGATATAAACAGGAACAGCAAATATTTATATTTTTTC ATAAATTTTCTAAATAAAAAGTTG

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FIGURE 126

MVELFIFLFLLGETPFKVVVKSLSPKELVRIHVPKPLDRNDGTFLMRYRMYETVDEGLKIEVL
YGDEHVAQSPYILKGPVYHEYCECPEDPQAWQKTLSCPTKEPQIAKDFASFPSINLQQMLKEV
PKRFGDERGAIVHYTILNNHVYRRSLGKYTDFKMFSDEILLSLTRKVLLPDLEFYVNLGDWPL
EHRKVNGTPSPIPIISWCGSLDSRDVVLPTYDITHSMLEAMRGVTNDLLSIQGNTGPSWINKT
ERAFFRGRDSREERLQLVQLSKENPQLLDAGITGYFFFQEKEKELGKAKLMGFFDFFKYKYQV
NVDGTVAAYRYPYLMLGDSLVLKQDSPYYEHFYMALEPWKHYVPIKRNLSDLLEKVKWAKEND
EEAKKIAKEGQLMARDLLQPHRLYCYYYQVLQKYAERQSSKPEVRDGMELVPQPEDSTAICQC
HRKKPSREEL

Important features of the protein:

Signal peptide:

amino acids 1-16

N-glycosylation sites.

amino acids 250-254, 363-367

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 444-448

N-myristoylation site.

amino acids 208-214, 319-325, 388-394

Endoplasmic reticulum targeting sequence.

amino acids 448-453

Mitochondrial energy transfer proteins signature.

amino acids 25-34

FIGURE 127

AGCCGTCGGAGGGAGCCGGAGCGCTTCTCCCGAGTTGGTGATAGATTGGTGGTCATCCAACAT GCAGAAATGAATGAGCAGTGAAAAGCAGCAGAGCCGATGGGTCATGAGGATGTAAGTGCGTTT GAAGGCTTCCACACCCTCTACTCCAGGAATCATGAATAAACTGGAGGATAAGCAGGACCAGAT GATACCATGAAGAGAAGTTTACAGGCCCTCTATTGCCAACTGTTAAGTTTCCTGCTGATCTTG GCACTGACCGAAGCGCTGGCATTTGCCATCCAGGAACCATCTCCCAGGGAATCTCTTCAGGTC CTCCCTTCAGGCACTCCCCGGGAACCATGGTGACAGCACCCCACAGCTCTACCAGACATACT TCTGTGGTGATGCTGACCCCCAATCCCGATGGACCCCCCTCACAGGCTGCAGCTCCCATGGCA ACACTGACACCCGTGCAGAGGGGCACCCTCCTACGCACACCATCTCCACCATCGCTGCGACA GTAACCGCCCCTATTCTGAAAGCTCCCTGTCCACAGGGCCCGCTCCAGCAGCCATGGCAACC ACATCCTCCAAGCCAGAGGGCCGCCCTCGAGGGCAGGCTGCCCCCACCATCCTGCTGACAAAG CCACCGGGGGCCACCAGCCCCCCACCACAGCGCCCCCCGCACTACCACACGCAGGCCCCCC AGGCCCCAGGCTCTTCCCGAAAAGGGGCTGGTAATTCATCACGCCCTGTCCCGCCTGCACCT GGTGGCCACTCCAGGAGTAAAGAAGGACAGCGAGGACGAAATCCAAGCTCCACACCTCTGGGG CAGAAGCGGCCCCTGGGGAAAATCTTTCAGATCTACAAGGGCAACTTCACAGGGTCTGTGGAA CCAGAGCCCTCTACCCTCACCCCAGGACCCCACTCTGGGGCTACTCCTCTTCACCACAGCCC GGGCCTGCAAAGGACAAGCCAGGCCTTCGCAGAGCAGCCCAGGGGGGTGGTTCTACCTTCACC AGCCAAGGAGGGACACCAGATGCCACAGCAGCCTCAGGTGCCCCTGTCAGTCCACAAGCTGCC CCAGTGCCTTCTCAGCGCCCCCACCACGGTGACCCACAGGATGGCCCCAGCCATAGTGACTCT TGGCTTACTGTTACCCCTGGCACCAGCAGACCTCTGTCTACCAGCTCTGGGGTCTTCACGGCT GCCACGGGGCCCACCCCAGCTGCCTTCGATACCAGTGTCTCAGCCCCTTCCCAGGGGATTCCT CAGGGAGCATCCACAACCCCACAAGCTCCAACCCATCCCTCCAGGGTCTCAGAAAGCACTATT TCCACAGTGGTATCCACAGCCACAGGCAATTTCCTCAACCGCCTGGTCCCCGCCGGGACCTGG AAGCCTGGGACAGCAGGGAACATCTCCCATGTGGCCGAGGGGGACAAACCGCAGCACAGAGCC ACCATCTGCCTGAGCAAGATGGATATCGCCTGGGTGATCCTGGCCATCAGCGTGCCCATCTCC AACAACCTGAGCTACTGGAACAACACCATCACCATGGACTACTTCAACAGGCATGCTGTGGAG CTGCCCAGGGAGATCCAGTCCCTTGAAACCTCTGAGGACCAGCTCTCAGAGCCCCGCTCCCCA GCCAATGGCGACTATAGAGACACTGGGATGGTCCTTGTTAACCCCTTCTGTCAAGAAACACTG TTTGTGGGAAACGATCAAGTATCTGAGATC<u>TAA</u>CTACAGCAGGCATCACTTTGCCATTCCGTA TGACTTAATGAGAAACATTTTCAGCTTTTTTTCCTATGAATTGTCAACATCTTTTTTACAAGT GTGGTTTAAAAAAAAAAAACTTTACAGAATGATCTGTGGCTTTATAAAATAAAGGTATTTCT AAGCAAAAAAAAAAAAAAAAA

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FIGURE 128

MKRSLQALYCQLLSFLLILALTEALAFAIQEPSPRESLQVLPSGTPPGTMVTAPHSSTRHTSV
VMLTPNPDGPPSQAAAPMATLTPRAEGHPPTHTISTIAATVTAPYSESSLSTGPAPAAMATTS
SKPEGRPRGQAAPTILLTKPPGATSRPTTAPPRTTTRRPPRPPGSSRKGAGNSSRPVPPAPGG
HSRSKEGQRGRNPSSTPLGQKRPLGKIFQIYKGNFTGSVEPEPSTLTPRTPLWGYSSSPQPQT
VAATTVPSNTSWAPTTTSLGPAKDKPGLRRAAQGGGSTFTSQGGTPDATAASGAPVSPQAAPV
PSQRPHHGDPQDGPSHSDSWLTVTPGTSRPLSTSSGVFTAATGPTPAAFDTSVSAPSQGIPQG
ASTTPQAPTHPSRVSESTISGAKEETVATLTMTDRVPSPLSTVVSTATGNFLNRLVPAGTWKP
GTAGNISHVAEGDKPQHRATICLSKMDIAWVILAISVPISSCSVLLTVCCMKRKKKTANPENN
LSYWNNTITMDYFNRHAVELPREIQSLETSEDQLSEPRSPANGDYRDTGMVLVNPFCQETLFV
GNDOVSEI

Important features of the protein:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 469-487

N-glycosylation sites.

amino acids 178-182, 223-227, 261-265, 446-450, 504-508, 509-513

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 495-499

N-myristoylation sites.

amino acids 44-50, 48-54, 175-181, 222-228, 279-285, 286-292, 288-294, 296-302, 351-357, 374-380, 427-433, 442-448

TonB-dependent receptor proteins signature 1.

amino acids 1-44

FIGURE 129

AGGCGAGGCGCGCCGCTGCACACACGCACACGGAGCTATGGGGTGCCATGTTGCCACCAG CTGCCACGTGGCCTGGCTTTTGGTGCTGATCTCTGGATGCTGGGGCCAGGTGAACCGGCTGCC CTTCTTCACCAACCACTTCTTTGATACATACCTGCTGATCAGCGAGGACACGCCTGTGGGTTC TTCTGTGACCCAGTTGCTGGCCCAAGACATGGACAATGACCCCCTGGTGTTTTGGCGTGTCTGG GGAGGAGGCCTCTCGCTTCTTTGCAGTGGAGCCTGACACTGGCGTGGTGTGGCTCCGGCAGCC ACTGGACAGAGACCAAGTCAGAGTTCACCGTGGAGTTCTCTGTCAGCGACCACCAGGGGGT GATCACACGGAAGGTGAACATCCAGGTCGGGGATGTGAATGACAACGCGCCCACATTTCACAA TCAGCCCTACAGCGTCCGCATCCCTGAGAATACACCAGTGGGGACGCCCATCTTCATCGTGAA TGCCACAGACCCCGACTTGGGGGCAGGGGGCAGCGTCCTCTACTCCTTCCAGCCCCCCTCCCA ATTCTTCGCCATTGACAGCGCCCGCGGTATCGTCACAGTGATCCGGGAGCTGGACTACGAGAC CACACAGGCCTACCÁGCTCACGGTCAACGCCACAGATCAAGACCAGGCCTCTGTCCAC CCTGGCCAACTTGGCCATCATCATCACAGATGTCCAGGACATGGACCCCATCTTCATCAACCT GCCTTACAGCACCAACATCTACGAGCATTCTCCTCCGGGCACGACGGTGCGCATCATCACCGC CATAGACCAGGATAAAGGACGTCCCCGGGGCATTGGCTACACCATCGTTTCAGGGAATACCAA CAGCATCTTTGCCCTGGACTACATCAGCGGAGTGCTGACCTTGAATGGCCTGCTGGACCGGGA GAACCCCTGTACAGCCATGGCTTCATCCTGACTGTGAAGGGCACGGAGCTGAACGATGACCG CACCCCATCTGACGCTACAGTCACCACGACCTTCAATATCCTGGTTATTGACATCAATGACAA TGCCCCGGAGTTCAACAGCTCCGAGTACAGCGTGGCCATCACTGAGCTGGCACAGGTCGGCTT TGCCCTTCCACTCTTCATCCAGGTGGTGGACAAGGATGAGAATTTGGGCCTGAACAGCATGTT TGAGGTGTACTTGGTGGGGAACAACTCCCACCACTTCATCATCTCCCCGACCTCCGTCCAGGG GAAGGCGGACATTCGTATTCGGGTGGCCATCCCACTGGACTACGAGACCGTGGACCGCTACGA CTTTGATCTCTTTGCCAATGAGAGTGTGCCTGACCATGTGGGCTATGCCAAGGTGAAGATCAC CGAGAACGTCACCGTGGGGACCTCTGTGCTGACAGTCCTGGTGAGTCCCCGCTTCACTGCAGG GCCACTGAGCTCTCCAGGGCCGACTGTGGTGAGGCACCCAGAGGGATTTTGTCCAAGGGACCT CAGCAATCAGGGAAGGAGCACCCCCAAATCCCTGAGCTGTTTTGTTGGTGTAT**TAA**ATAAA GTTTTTGGACTCTTCAGGAAGGGGCTCCCTTGACCTAGGTTGCAATATGGAAAAGGAGCCAAC AGAAGGGCAACCCTCTCCATGTGAGCACAGGCACCAGAGAGGGGCAGGCGCCTGGAGGGTACC GGGGCACCCCAGCTGCCCATGGCTGGACTTGCCCTTTGACAAGGGGCCCTCCCAGTGTCATT TGTATCTGTCAGTACTCTTGGTTGCAAGGGACAGAAACCCTTAAGTAGTTCAAGCAAAAAAGG ATTGGCTCATGTAACTCAAAAGTATAAGTGATTTCAGGCCGGGCTCGGTGGCTCACGCCTGTC ATCCAACACCTTGAGAAAGCCGAGGTGGGCGGATCACTTGAGGTCGGGAGTTTGAGACCAGCC TGGCCAACATGGCAAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGTGTGGTGGCAC ACGCCTGTAGTCCCAGCTACTAGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCGG AGGTTGCAGTGAGCCGAGATTGTGTCACTGCCCTCCAGCCTGGGCGACAGAGCCAGATTCTGT CTC

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FIGURE 130

MGCHVATSCHVAWLLVLISGCWGQVNRLPFFTNHFFDTYLLISEDTPVGSSVTQLLAQDMDND PLVFGVSGEEASRFFAVEPDTGVVWLRQPLDRETKSEFTVEFSVSDHQGVITRKVNIQVGDVN DNAPTFHNQPYSVRIPENTPVGTPIFIVNATDPDLGAGGSVLYSFQPPSQFFAIDSARGIVTV IRELDYETTQAYQLTVNATDQDKTRPLSTLANLAIIITDVQDMDPIFINLPYSTNIYEHSPPG TTVRIITAIDQDKGRPRGIGYTIVSGNTNSIFALDYISGVLTLNGLLDRENPLYSHGFILTVK GTELNDDRTPSDATVTTTFNILVIDINDNAPEFNSSEYSVAITELAQVGFALPLFIQVVDKDE NLGLNSMFEVYLVGNNSHHFIISPTSVQGKADIRIRVAIPLDYETVDRYDFDLFANESVPDHV GYAKVKITLINENDNRPIFSQPLYNISLYENVTVGTSVLTVLVSPRFTAGPLSSPGPTVVRHP EGFCPRDLSNOGRRHPOIPELCLLVY

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 355-374

N-glycosylation sites.

amino acids 155-159, 206-210, 349-353, 393-397, 434-438, 466-470, 472-476

N-myristoylation sites.

amino acids 2-8, 49-55, 162-168, 270-276, 278-284, 316-322

Amidation site.

amino acids 515-519

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 11-22

Leucine zipper pattern.

amino acids 298-320

PTS HPR component serine phosphorylation site signature.

amino acids 377-393

Cadherins extracellular repeated domain signature.

amino acids 120-131, 336-347

Cadherins extracellular

amino acids 120-144, 336-360

FIGURE 131

GTGGGCCGCCCTGCTGCCGTCCATGCTGATGTTTGCGGTGATCGTGGCCTCCAGCGGGC GCCGCGAGGGCACAGCCTGGCGCGGGAAAGCCCCCAAGCCTGGGGGCCTGTCCCTCAGGGCTG AGCCAGGCATGCCCCGGGACCCCTGGGACTTGCCGGTGGGGCAGCGGCGCACCCTGCTGCGCC ACATCCTCGTAAGTGACCGTTACCGCTTCCTCTACTGCTACGTCCCCAAGGTGGCCTGCTCTA ACTGGAAGCGGGTGATGAAGGTGCTGGCAGGCGTCCTGGACAGCGTGGACGTCCGCCTCAAGA TGGACCACCGCAGTGACCTGGTGTTCCTGGCCGACCTGCGGCCTGAGGAGATTCGCTACCGCC TGCAGCACTACTTTAAGTTCCTGTTTGTGCGGGAGCCCTTGGAACGCCTCCTCTCTGCCTACC GCAACAAGTTTGGCGAGATCCGAGAGTACCAGCAACGCTATGGGGCTGAGATAGTGAGGCGGT ACAGGGCTGGAGCGGGCCCAGCCCTGCAGGCGACGATGTCACATTCCCCGAGTTCCTGAGAT ACCTGGTGGATGAGGACCCTGAGCGCATGAATGAGCATTGGATGCCCGTGTACCACCTGTGCC AGCCTTGTGCCGTGCACTATGACTTTGTGGGCTCCTATGAGAGGCTGGAGGCTGATGCAAATC AGGTGCTGGAGTGGGTACGGCCACCTCACGTCCGATTTCCAGCTCGCCAGGCCTGGTACC GGCCAGCCAGCCCGAAAGCCTGCATTACCACTTGTGCAGTGCCCCCGGGCCCTGCTGCAGG ATGTGCTGCCTAAGTATATCCTGGACTTCTCCCTCTTTGCCTACCCACTGCCTAATGTCACCA AGGAGGCGTGTCAGCAG**TGA**CCATGGGTGTGGGGCCAGCAGCTGGTGGGGACTGGTTTCAACG CCAGCTTTCTGTGCTTCTGCCTGTCATTCGGAGAAACTCTGGCTCTGGGGCTTGGGGCTTCTC AGGATCCTGGATGGCAGAGACTGCCCTCAGAAGTTCCTTGTCCAGGGTGGGCACCCACAGTGA CTCAGAGGACAGGGCTAGGCAGGAGACCTGCTGCTCCTCATTGGGGGGGATCTCTTGGGGGGGCA GACACCAGTTTGCCAATGAAGCAACACATCTGATCTAAAGACTGGCTCCAGACCCCGGGCTGC CAGGATTATGCAGTCCACTTGGTCTACCTTAATTTAACCTGTGGCCAAACTCAGAGATGGTAC CAGCCAGGGGCAAGCATGACCAGAGCCAGGGACCCTGTGGCTCTGATCCCCCATTTATCCACC CCATGTGCCTCAGGACTAGAGTGAGCAATCATACCTTATAAATGACTTTTGTGCCTTTCTGCT CCAGTCTCAAAATTTCCTACACCTGCCAGTTCTTTACATTTTTCCAAGGAAAGGAAAACGGAA GCAGGGTTCTTGCCTGGTAGCTCCAGGACCCAGCTCTGCAGGCACCCAAAGACCCTCTGTGCC TGTACTTTTGATAGAACCCTTGTAAGGGCTTTGTTTTCCTAATAGCTGACTTTTTAATAAAG CAGTTTTATATAT

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FIGURE 132

MLMFAVIVASSGLLLMIERGILAEMKPLPLHPPGREGTAWRGKAPKPGGLSLRAGDADLQVRQ DVRNRTLRAVCGQPGMPRDPWDLPVGQRRTLLRHILVSDRYRFLYCYVPKVACSNWKRVMKVL AGVLDSVDVRLKMDHRSDLVFLADLRPEEIRYRLQHYFKFLFVREPLERLLSAYRNKFGEIRE YQQRYGAEIVRRYRAGAGPSPAGDDVTFPEFLRYLVDEDPERMNEHWMPVYHLCQPCAVHYDF VGSYERLEADANQVLEWVRAPPHVRFPARQAWYRPASPESLHYHLCSAPRALLQDVLPKYILD FSLFAYPLPNVTKEACQQ

Important features of the protein:

Signal peptide:

amino acids 1-23

N-glycosylation sites.

amino acids 67-71, 325-329

Tyrosine kinase phosphorylation sites.

amino acids 152-159, 183-183

N-myristoylation sites.

amino acids 89-95, 128-134

FIGURE 133

CGGCAGTTCTGGCCCCTGCAGCTGGAGGTACCCTGAGTTCTGAGGGTCGTAGTGCTGTTTCTG GTATTCTCATCGCGGTCACCTCTACCGGTGTGGACAAGTAAAGTTTGAATCAGCTTCTCCATG GCCTGGGCACCAGTTCCCGGCTGAGCCATTTTCCTTTTGGCTAAAAGTCCCCGCCCAGAGGCC AATTCGTCGCGGCGGTGGAGATCGCAGGTCGCTCAGGCTTGCAGATCGGTCAAGGGTTGT GGAGAGTGGTCAGAAACCAGCAGCTGCAACAAGAAGGCTACAGTGAGCAAGGCTACCTCACCA GAGAGCAGAGCAGAGAATGGATGCGAGCAACATTTCTAACACCAATCATCGTAAACAAGTCC TTAATTTGGAAATGTTGCCTCCTGAGCTAAGCTTTACCATCTTGTCCTACCTGAATGCAACTG ACCTTTGCTTGGCTTCATGTGTTTTGGCAGGACCTTGCGAATGATGAACTTCTCTGGCAAGGGT TGTGCAAATCCACTTGGGGTCACTGTTCCATATACAATAAGAACCCACCTTTAGGATTTTCTT TTAGAAAATTGTATATGCAGCTGGATGAAGGCAGCCTCACCTTTAATGCCAACCCAGATGAGG GAGTGAACTACTTTATGTCCAAGGGTATCCTGGATGATTCGCCAAAGGAAATAGCAAAGTTTA TCTTGGATGACCTTGTAACATTGCATAATTTTAGAAATCAGTTCTTGCCAAATGCACTGAGAG AATTTTTTCGTCATATCCATGCCCCTGAAGAGCGTGGAGAGTATCTTGAAACTCTTATAACAA AGTTCTCACATAGATTCTGTGCTTGCAACCCTGATTTAATGCGAGAACTTGGCCTTAGTCCTG ATGCTGTCTATGTACTGTGCTACTCTTTGATTCTACTTTCCATTGACCTCACTAGCCCTCATG TGAAGAATAAAATGTCAAAAAGGGAATTTATTCGAAATACCCGTCGCGCTGCTCAAAATATTA GTGAAGATTTTGTAGGGCATCTTTATGACAATATCTACCTTATTGGCCATGTGGCTGCA**TAA**A AAGCACAATTGCTAGGACTTCAGTTTTTACTTCAGACTAAAGCTACCCAAGGACTTAGCAGAT ATGGGGGTTACATCAGTGCTGGTCATTGTAGCCTGAGTATACAATCAAGCTTCAGTGTGCAAC CTTTTTTTTTTTTTCCATTTTCTATTTTAGTAATTTCCTTGGGGAACTAAATAATTTTGCAGA ATTTTTCCTAATTTTGTTTATCACGTTTTGCACAAAGCAGAGCCACTGTCTAACACAGCTGTT AACGAATGATAAACTGACATTATACTCTAAAAGATGGTGTATTTGTGCATTAGATTTGCCTGA AAAACTTTATCCATTTCCATTCTTTATACAAATACCATGTAATGTGTACATATTTAACTAAAG AGATTTATAGTCATAATTATTTTATTGTAAAGATTTTAACTAAAGTTTTTCCTTTTCTCTC

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FIGURE 134

MGQGLWRVVRNQQLQQEGYSEQGYLTREQSRRMDASNISNTNHRKQVQGGIDIYHLLKARKSK EQEGFINLEMLPPELSFTILSYLNATDLCLASCVWQDLANDELLWQGLCKSTWGHCSIYNKNP PLGFSFRKLYMQLDEGSLTFNANPDEGVNYFMSKGILDDSPKEIAKFIFCTRTLNWKKLRIYL DERRDVLDDLVTLHNFRNQFLPNALREFFRHIHAPEERGEYLETLITKFSHRFCACNPDLMRE LGLSPDAVYVLCYSLILLSIDLTSPHVKNKMSKREFIRNTRRAAQNISEDFVGHLYDNIYLIG HVAA

Important features of the protein:

Transmembrane domain:

amino acids 253-272

N-glycosylation sites.

amino acids 37-41, 87-91, 298-302

N-myristoylation site.

amino acids 110-116

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FIGURE 135

GGCACGAGGGAGCCTCCGTTAGGGGGTGGGAAAGGACTTTGCCATAGGTCGCTGAGGCCACCA TCTGCTCTCTTACTGGCCAAGGGCGTAAAAAGATAGTCTTCCCATTAGCTAGAGAGCAAACCC CAGAAAGCCTATTGGCTGCGCCGTCCGCGGGCCTTGGTCCGCTTTGAAGGCGGGCTGCGGCTG CGAGAGGAGGCGGGGGGGGGGCTAGCTGTTGTCGTGGTTGCTCGGAGGCACGTGTGCAGTCC CGGAAGCGGCGAGGGAAACTGCTCCGCGCGCGCGCGGGAGGAGGAACCGCCCGGTCCTTTA GGGTCCGGGCCGGCCGGGCCATGGATTCAATGCCTGAGCCCGCGTCCCGCTGTCTTCTGCTT CTTCCCTTGCTGCTGCTGCTGCTGCTGCTGCCGGCCCCGGAGCTGGGCCCGAGCCAGGCC GGAGCTGAGGAGAACGACTGGGTTCGCCTGCCCAGCAAATGCGAAGTGTGTAAATATGTTGCT GTGGAGCTGAAGTCAGCCTTTGAGGAAACCGGCAAGACCAAGGAGGTGATTGGCACGGGCTAT GGCATCCTGGACCAGAAGGCCTCTGGAGTCAAATACACCAAGTCGGACTTGCGGTTAATCGAA GTCACTGAGACCATTTGCAAGAGGCTCCTGGATTATAGCCTGCACAAGGAGAGGACCGGCAGC AATCGATTTGCCAAGGGCATGTCAGAGACCTTTGAGACATTACACAACCTGGTACACAAAGGG GTCAAGGTGGTGATGGACATCCCCTATGAGCTGTGGAACGAGACTTCTGCAGAGGTGGCTGAC CTCAAGAAGCAGTGTGATGTGCTGGTGGAAGAGTTTGAGGAGGTGATCGAGGACTGGTACAGG AACCACCAGGAGGAAGACCTGACTGAATTCCTCTGCGCCAACCACGTGCTGAAGGGAAAAGAC AAGTCCAAGAAGAAGAGCAGCAGGGCCAAGGCAGCAGGCGGCAGGAGTAGCAGCAAACAA AGGAAGGAGCTGGGTGGCCTTGAGGGAGACCCCAGCCCCGAGGAGGATGAGGGCATCCAGAAG AGACCCCTGATTTTGAAGCTGAGGAGTCAGGGGCATGGCTCTGGCAGGCCGGGATGGCCCCGC AGCCTTCAGCCCCTCCTTGCCTTGGCTGTGCCCTCTTCTGCCAAGGAAAGACACAAGCCCCAG GAAGAACTCAGAGCCGTCATGGGTAGCCCACGCCGTCCTTTCCCCTCCCCAAGTGTTTCTCTC CTGACCCAGGGTTCAGGCAGGCCTTGTGGTTTCAGGACTGCAAGGACTCCAGTGTGAACTCAG GAGGGGCAGGTGTCAGAACTGGGCACCAGGACTGGAGCCCCCTCCGGAGACCAAACTCACCAT CCCTCAGTCCTCCCCAACAGGGTACTAGGACTGCAGCCCCCTGTAGCTCCTCTCTGCTTACCC CTCCTGTGGACACCTTGCACTCTGCCTGGCCCTTCCCAGAGCCCAAAGAGTAAAAATGTTCTG GTTCTGATTTCTGAAAAAAAAAAAAAAAAAAAAAATTCCT

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FIGURE 136

MDSMPEPASRCLLLLPLLLLLLLLLPAPELGPSQAGAEENDWVRLPSKCEVCKYVAVELKSAF EETGKTKEVIGTGYGILDQKASGVKYTKSDLRLIEVTETICKRLLDYSLHKERTGSNRFAKGM SETFETLHNLVHKGVKVVMDIPYELWNETSAEVADLKKQCDVLVEEFEEVIEDWYRNHQEEDL TEFLCANHVLKGKDTSCLAEQWSGKKGDTAALGGKKSKKKSSRAKAAGGRSSSSKQRKELGGL EGDPSPEEDEGIOKASPLTHSPPDEL

Important features of the protein:

Signal peptide:

amino acids 1-26

N-glycosylation site.

amino acids 153-157

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 227-231, 228-232

Tyrosine kinase phosphorylation site.

amino acids 142-150

N-myristoylation sites.

amino acids 36-42, 74-80, 86-92, 125-131, 222-228, 237-243, 250-256, 263-269

Amidation sites.

amino acids 212-216, 222-226

ATP/GTP-binding site motif A (P-loop).

amino acids 62-70

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FIGURE 137

CACGCCTCCCGCTGCCAGCCCGGCACCGGGATCTTAATCAGTCACTATGAAAACTCATTAGCT CCACAGCA**TG**AGTCCTCCACTGCTGAAGCTTGGCGCTGTGCTTAGTACCATGGCAATGATCT CAAACTGGATGTCCCAAACTCTCCCATCCTTGGTGGGACTGAACACCACGAGGCTGTCGACTC CGGATACCTTAACTCAGATTAGTCCTAAAGAAGGGTGGCAGGTGTACAGCTCAGCTCAGGATC CTGATGGGCGGTGCATTTGCACAGTTGTTGCTCCAGAACAAAACCTGTGTTCCCGGGATGCCA AAAGCAGGCAACTTCGCCAACTACTGGAAAAGGTTCAGAACATGTCCCAGTCTATTGAAGTCT TAAACTTGAGAACTCAGAGAGATTTCCAATATGTTTTAAAAATGGAAACCCAAATGAAAGGGC TGAAGGCAAAATTTCGGCAGATTGAAGATGATCGAAAGACACTTATGACCAAGCATTTTCAGG AGTTGAAAGAGAAAATGGACGAGCTCCTGCCTTTGATCCCCGTGCTGGAACAGTACAAAACAG TTCAGGAGGAAATTGGTGCCTATGACTACGAGGAACTACACCAAAGAGTGCTGAGCTTGGAAA CAAGACTTCGTGACTGCATGAAAAAGCTAACATGTGGCAAACTGATGAAAATCACAGGCCCAG TTACAGTCAAGACATCTGGAACCCGATTTGGTGCTTGGATGACAGACCCTTTAGCATCTGAGA AAAACAACAGAGTCTGGTACATGGACAGTTATACTAACAATAAAATTGTTCGTGAATACAAAT GAACTAACCATGTTGTCTACAATGGCTCACTCTATTTTAACAAGTATCAGAGTAATATCATCA TCAAATACAGCTTTGATATGGGGAGAGTGCTTGCCCAACGAAGCCTGGAGTATGCTGGTTTTC ATAATGTTTACCCCTACACATGGGGTGGATTCTCTGACATCGACCTAATGGCTGATGAAATCG GGCTGTGGGCTGTATGCAACTAACCAGAATGCAGGCAATATTGTCATCAGCCAACTTAACC AAGATACCTTGGAGGTGATGAAGAGCTGGAGCACTGGCTACCCCAAGAGAAGTGCAGGGGAAT CTTTCATGATCTGTGGGACACTGTATGTCACCAACTCCCACTTAACTGGAGCCAAGGTGTATT ATTCCTATTCCACCAAAACCTCCACATATGAGTACACAGACATTCCCTTCCATAACCAATACT TTCACATATCCATGCTTGACTACAATGCAAGAGATCGAGCTCTCTATGCCTGGAACAATGGCC ACCAGGTGCTGTTCAATGTCACCCTTTTCCATATCATCAAGACAGAGGATGACACA**TAG**GCAA ATGTGACATGTTTTCATTGATTTAAACAGTGTGATTTGTGATAAACTCTATAAGACCCCTTCC GTTTTTTTCTTCACTATTATTTTTCATCATTTCTCCAAAGCAAAGCATTTTTATTGTAAAGTT GGTGTTTCAAAAACATAGCTGAGCTTGTCTAACTTACCATGTTGGAAACACATCTTAACTTCT GGCTAAAGTCATAGTTTTGCAAGAGATTAATGATCTGCCTTATATTAGAGTCAGAGACTAATG GTGGCTTAAATGCACGAATGTCTTTTTTTTTAAAACTGTCATTTTTTAACTGTCTTTTTGCTCCA TAAAAAATGTAAGGATTTCATTTATATTGAAAAATAATATTAATCATTTTGCTGTTAACACAA TTCTCTGATGCGGTGCTGTACAGTCATTTTTAAATCTCTTGCTAACATTTTATTGGCAGTATG

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FIGURE 138

MSPPLLKLGAVLSTMAMISNWMSQTLPSLVGLNTTRLSTPDTLTQISPKEGWQVYSSAQDPDG
RCICTVVAPEQNLCSRDAKSRQLRQLLEKVQNMSQSIEVLNLRTQRDFQYVLKMETQMKGLKA
KFRQIEDDRKTLMTKHFQELKEKMDELLPLIPVLEQYKTDAKLITQFKEEIRNLSAVLTGIQE
EIGAYDYEELHQRVLSLETRLRDCMKKLTCGKLMKITGPVTVKTSGTRFGAWMTDPLASEKNN
RVWYMDSYTNNKIVREYKSIADFVSGAESRTYNLPFKWAGTNHVVYNGSLYFNKYQSNIIIKY
SFDMGRVLAQRSLEYAGFHNVYPYTWGGFSDIDLMADEIGLWAVYATNQNAGNIVISQLNQDT
LEVMKSWSTGYPKRSAGESFMICGTLYVTNSHLTGAKVYYSYSTKTSTYEYTDIPFHNQYFHI
SMLDYNARDRALYAWNNGHQVLFNVTLFHIIKTEDDT

Important features of the protein:

Signal peptide:

amino acids 1-16

N-glycosylation sites.

amino acids 33-37, 95-99, 179-183, 299-303, 465-469

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 215-219

Tyrosine kinase phosphorylation site.

amino acids 106-114

N-myristoylation sites.

amino acids 9-15, 31-37, 235-241, 239-245

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FIGURE 139

GAAGCAGTGCAGAGAGGAGAGCGGAGCCGGAGCTGCCGCTGAGCAAAGGCCTTCACCATGCCCG AGTCCCCGGCTGCTCCGTCTGGGCCCGCTGCCTCCACTGCCTGTATAGCTGCCACTGGA GGAAATGCCCCAGAGAGAGGATGCAAACCAGCAAGTGCGACTGTATCTGGTTTGGCCTGCTCT TCCTCACCTTCCTCCTTTCCCTGAGCTGGCTGTACATCGGGCTCGTCCTTCTCAATGACCTGC TGCTGGTCATCTCTCTACTGGTCACATATGCATCCTTGCTATTGGTCCTGGCCCTGCTCCTGC GGCTTTGTAGACAGCCCTGCATCTGCACAGCCTCCACAAGGTGCTGCTGCTCCTCATTATGC TGCTTGTGGCGCCTGGCCTTGTGGGACTGGACATCCAATGGCAGCAGGAGTGGCATAGCTTGC GTGTGTCACTGCAGGCCACAGCCCCATTCCTTCATATTGGAGCAGCCGCTGGAATTGCCCTCC TGGCCTGGCCTGTGGCTGATACCTTCTACCGTATCCACCGAAGAGGTCCCAAGATTCTGCTAC TGCTCCTATTTTTTGGAGTTGTCCTGGTCATCTACTTGGCCCCCCTATGCATCTCCTCACCCT GCATCATGGAACCCAGAGACTTACCACCCAAGCCTGGGCTGGTGGGACACCGAGGGCCCCCA TGCTGGCTCCCGAGAACACCCTGATGTCCTTGCGGAAGACAGCTGAATGCGGAGCTACTGTGT GCAGGACCACGAATGTAGCCTCTGTATTCCCAACCCGAATCACAGCCCACAGCAGTGACTTCT CCTGGACTGAACTGAAGAGCTCAATGCTGGATCCTGGTTCCTAGAGAGGCGACCCTTCTGGG GGGCCAAACCGCTGGCAGGCCCTGATCAGAAAGAGGCTGAGAGTCAGACGGTACCAGCATTAG AAGAGCTATTGGAGGAAGCTGCAGCCCTCAACCTTTCCATCATGTTCGACTTGCGCCGACCCC CACAGAACCACACATACTATGACACTTTTGTGATCCAGACATTGGAGACTGTGCTGAATGCAA GGGTGCCCCAAGCCATGGTCTTTTGGCTACCAGATGAAGATCGGGCTAATGTCCAACGACGG CACCTGGAATGCGCCAGATATATGGACGTCAGGGAGGCCAACAGAACGGAGAGGCCCCAGTTTC TTAACCTCCCCTATCAAGATCTGCCACTATTGGATATCAAGGCATTGCATAAGGATAATGTCT CGGTGAACCTATTTGTAGTGAACAAGCCCTGGCTCTTCTCTCTGCTTTGGTGTGCAGGGGTGG ATTCGGTCACCACCAACGACTGCCAGCTGCTGCAGCAGATGCGTTACCCTATCTGGCTTATTA CCCCTCAAACCTACCTAATCATATGGGTCATTACCAATTGTGTTTCCACCATGCTGCTTTTGT GGACCTTCCTCCTCCAAAGGAGATTTGTTAAGAAGAGAGGGAAAACTGGCTTAGAAACAGCAG TGCTGCTGACAAGGATCAACAATTTCATGATGGAG<u>TGA</u>ATGCCCTGCCCTGCTTCCCCACCCA AGCCAGTCTACATTGCCCAAACAGCAAGGGTTGGAGAGTGGCTTAAGTGGAATGCTTCAGGGG TGGTGGGTTGCAAGTGGGGGGAGCTTTGCCAACAGGAGGTTTTGAACCATGAGGGCCCTCTGC CCAGGTGATGGGCATTCCCTAAGCTGCTATGGAATCTGCTCCCTTTGGGGTTTTTGACCTGAGA TGTTTGGGAAGAGTGAGTAATGAGAAGTTTCTCCTCAAATGAAACTAGAACAGGGAAGTA AAAGGGAGATTGCTCGGA

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FIGURE 140

MAESPGCCSVWARCLHCLYSCHWRKCPRERMQTSKCDCIWFGLLFLTFLLSLSWLYIGLVLLN
DLHNFNEFLFRRWGHWMDWSLAFLLVISLLVTYASLLLVLALLLRLCRQPLHLHSLHKVLLLL
IMLLVAAGLVGLDIQWQQEWHSLRVSLQATAPFLHIGAAAGIALLAWPVADTFYRIHRRGPKI
LLLLLFFGVVLVIYLAPLCISSPCIMEPRDLPPKPGLVGHRGAPMLAPENTLMSLRKTAECGA
TVFETDVMVSSDGVPFLMHDEHLSRTTNVASVFPTRITAHSSDFSWTELKRLNAGSWFLERRP
FWGAKPLAGPDQKEAESQTVPALEELLEEAAALNLSIMFDLRRPPQNHTYYDTFVIQTLETVL
NARVPQAMVFWLPDEDRANVQRRAPGMRQIYGRQGGNRTERPQFLNLPYQDLPLLDIKALHKD
NVSVNLFVVNKPWLFSLLWCAGVDSVTTNDCQLLQQMRYPIWLITPQTYLIIWVITNCVSTML
LLWTFLLQRRFVKKRGKTGLETAVLLTRINNFMME

Important features of the protein:

Transmembrane domains:

amino acids 38-60, 83-107, 122-138, 156-173, 189-210, 484-506

N-glycosylation sites.

amino acids 349-353, 362-366, 415-419, 442-446

N-myristoylation sites.

amino acids 163-169, 413-419, 523-529

Leucine zipper pattern.

amino acids 93-115, 109-131

Glutamine amidotransferases class-II active site.

amino acids 1-13

FIGURE 141

GCCGCCGGCCGGGCTGGAGCCGAGCGCAGCAGCCACCGCCGCCGCCGCCAGAAGTTTGGGTTGAACCGGAGC GCGCTCCGGCACCCGGGCGCTGGTCTGCCCTGTGACGAGTCCAAGTGCGAGGAGCCCAGGAACTGCCCGGG CGGGATTTACGGAACCTGCGACCGGGGGCTGCGTTGTGTCATCCGCCCCCGCTCAATGGCGACTCCCTCACCGA GTACGAAGCGGGCGTTTGCGAAGATGAGAACTGGACTGATGACCAACTGCTTGGTTTTAAACCATGCAATGAAAA CCTTATTGCTGGCTGCAATATAATCAATGGGAAATGTGAATGTAACACCATTCGAACCTGCAGCAATCCCTTTGA GTTTCCAAGTCAGGATATGTGCCTTTCAGCTTTAAAGAGAATTGAAGAAGAGAAGCCAGATTGCTCCAAGGCCCG CTGTGAAGTCCAGTTCTCCCACGTTGTCCTGAAGATTCTGTTCTGATCGAGGGTTATGCTCCTCCTGGGGAGTG CTGTCCCTTACCCAGCCGCTGCGTGTGCAACCCCGCAGGCTGTCTGCGCAAAGTCTGCCAGCCGGGAAACCTGAA CATACTAGTGTCAAAAGCCTCAGGGAAGCCGGGAGAGTGCTGTGACCTCTATGAGTGCAAACCAGTTTTCGGCGT GGACTGCAGGACTGTGGAATGCCCTCCTGTTCAGCAGACCGCGTGTCCCCCGGACAGCTATGAAACTCAAGTCAG ${\tt ACTAACTGCAGATGGTTGCTGTACTTTGCCAACAAGATGCGAGTGTCTCTCTGGCTTATGTGGTTTTCCCCGTGTG}$ TGTTAATGATACAAAGCCAGCCTGCGTATTTAACAATGTGGAATATTATGATGGAGACATGTTTCGAATGGACAA $\tt CGGTGAACGCCACTGCGTTGCGACCGTCTGCGGACAGACCTGCACAAACCCTGTGAAAGTGCCTGGGGAGTGTTG$ CCCTGTGTGCGAAGAACCAACCATCATCACAGTTGATCCACCTGCATGTGGGGAGTTATCAAACTGCACTCTGAC AGGGAAGGACTGCATTAATGGTTTCAAACGCGATCACAATGGTTGTCGGACCTGTCAGTGCATAAACACCGAGGA ACTATGTTCAGAACGTAAACAAGGCTGCACCTTGAACTGTCCCTTCGGTTTCCTTACTGATGCCCAAAACTGTGA GATCTGTGAGTGCCGCCCAAGGCCCCAAGAAGTGCAGACCCATAATCTGTGACAAGTATTGTCCACTTGGATTGCT GAAGAATAAGCACGGCTGTGACATCTGTCGCTGTAAGAAATGTCCAGAGCTCTCATGCAGTAAGATCTGCCCCTT GGGTTTCCAGCAGGACAGTCACGGCTGTCTTATCTGCAAGTGCAGAGAGGCCTCTGCTTCAGCTGGGCCACCCAT CCTGTCGGGCACTTGTCTCACCGTGGATGGTCATCATCATAAAAATGAGGAGAGCTGGCACGATGGGTGCCGGGA ATGCTACTGTCTCAATGGACGGGAAATGTGTGCCCTGATCACCTGCCCGGTGCCTGTCGCGAACCCCACCAT TTGCCACGCCCCTGGAGGAGTACTTTGTGGAAGGAGAAACGTGGAACATTGACTCCTGTACTCAGTGCACCTG CCACAGCGGACGGGTGCTGTGTGAGACAGAGGTGTGCCCACCGCTGCTCTGCCAGAACCCCTCACGCACCCAGGA ${\tt CAAAAATGATGAAGGGGATATATTCCTGGCAGCTGAGTCCTGGAAGCCTGACGTTTGTACCAGCTGCATCTGC$ TGATAGCGTAATTAGCTGTTTCTCTGAGTCCTGCCCTTCTGTATCCTGTGAAAAGACCTGTCTTGAGAAAAGGCCA GTGTTGTCCCTACTGCATAGAAGACACAATTCCAAAGAAGGTGGTGTGCCACTTCAGTGGGAAGGCCTATGCCGA $\verb|CCCAGAACCAATCATACCCATTGAGAAGACAAACCATCGAGGAGGGTTGACCTGGAGGTTCCCCTGTGGCC| \\$ CACGCCTAGTGAAAATGATATCGTCCATCTCCCTAGAGATATGGGTCACCTCCAGGTAGATTACAGAGATAACAG GCTGCACCCAAGTGAAGATTCTTCACTGGACTCCATTGCCTCAGTTGTGGTTCCCATAATTATATGCCTCTCTAT TATAATAGCATTCCTATTCATCAATCAGAAGAAACAGTGGATACCACTGCTTTGCTGGTATCGAACACCAACTAA GCCTTCTTCCTTAAATAATCAGCTAGTATCTGTGGACTGCAAGAAAGGAACCAGAGTCCAGGTGGACAGTTCCCA GAGAATGCTAAGAATTGCAGAACCAGATGCAAGATTCAGTGGCTTCTACAGCATGCAAAAACAGAACCATCTACA ${\tt GGCAGACAATTTCTACCAAACAGTG} {\color{red}{\bf TGA}} {\tt AGAAAGGCAACTAGGATGAGGTTTCAAAAGACGGAAGACGACTAAAT}$ $\mathtt{CTGCTCTAAAAAGTAAACTAGAATTTGTGCACTTGCTTAGTGGATTGTATTGGATTGTACTGATGTACAGCGC}$ TAAGACCTTACTGGGATGGGCTCTGTCTACAGCAATGTGCAGAACAAGCATTCCCACTTTTCCTCAAAAAA

FIGURE 142

MYLVAGDRGLAGCGHLLVSLLGLLLLLARSGTRALVCLPCDESKCEEPRNCPGSIVOGVCGCC YTCASQRNESCGGTFGIYGTCDRGLRCVIRPPLNGDSLTEYEAGVCEDENWTDDQLLGFKPCN ENLIAGONIINGKCECNTIRTCSNPFEFPSQDMCLSALKRIEEEKPDCSKARCEVQFSPRCPE DSVLIEGYAPPGECCPLPSRCVCNPAGCLRKVCQPGNLNILVSKASGKPGECCDLYECKPVFG VDCRTVECPPVQQTACPPDSYETQVRLTADGCCTLPTRCECLSGLCGFPVCEVGSTPRIVSRG DGTPGKCCDVFECVNDTKPACVFNNVEYYDGDMFRMDNCRFCRCQGGVAICFTAQCGEINCER YYVPEGECCPVCEDPVYPFNNPAGCYANGLILAHGDRWREDDCTFCQCVNGERHCVATVCGQT CTNPVKVPGECCPVCEEPTIITVDPPACGELSNCTLTGKDCINGFKRDHNGCRTCQCINTEEL CSERKQGCTLNCPFGFLTDAQNCEICECRPRPKKCRPIICDKYCPLGLLKNKHGCDICRCKKC PELSCSKICPLGFQQDSHGCLICKCREASASAGPPILSGTCLTVDGHHHKNEESWHDGCRECY CLNGREMCALITCPVPACGNPTIHPGQCCPSCADDFVVQKPELSTPSICHAPGGEYFVEGETW NIDSCTQCTCHSGRVLCETEVCPPLLCQNPSRTQDSCCPQCTDQPFRPSLSRNNSVPNYCKND EGDIFLAAESWKPDVCTSCICIDSVISCFSESCPSVSCERPVLRKGQCCPYCIEDTIPKKVVC HFSGKAYADEERWDLDSCTHCYCLQGQTLCSTVSCPPLPCVEPINVEGSCCPMCPEMYVPEPT NIPIEKTNHRGEVDLEVPLWPTPSENDIVHLPRDMGHLQVDYRDNRLHPSEDSSLDSIASVVV PIIICLSIIIAFLFINQKKQWIPLLCWYRTPTKPSSLNNQLVSVDCKKGTRVQVDSSQRMLRI AEPDARFSGFYSMQKQNHLQADNFYQTV

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 940-962

N-glycosylation sites.

amino acids 71-75, 113-117, 330-334, 474-478, 746-750

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 992-996

N-myristoylation site.

amino acids 9-15, 58-64, 61-67, 75-81, 79-85, 362-368, 402-408, 407-413, 439-445, 492-498, 511-517, 551-557, 558-564, 586-592, 606-612, 625-631, 845-851

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 52-63, 844-855

Cell attachment sequence.

amino acids 314-317

Leucine zipper pattern.

amino acids 3-25

Eukaryotic thiol (cysteine) proteases cysteine active site.

amino acids 57-69

VWFC domain proteins.

amino acids 448-456, 382-390

C-terminal cystine knot proteins

amino acids 60-86

FIGURE 143

GACGTCTGGCCGGCTCCCGGCGAAGGGCAGCGGAGGAGCGCCCAGAGCGCCAGCTAGGGCA GGTCCCGGGCGCGGCTGACTGCCGGCTGGTTCCCTGCGCGCAGTAGCTCCCCGAGCCGGGCTG ${\tt CACCGGAGGCGGGGAG{\color{red}{\bf ATG}}GTCGCGCGCGTCGGCCTCCTGCTGCGCGCCCTGCAGCTGCTACT}$ GTGGGGCCACCTGGACGCCCAGCCCGCGGAGCGCGGAGGCCAGGAGCTGCGCAAGGAGGCGGA GGCATTCCTAGAGAAGTACGGATACCTCAATGAACAGGTCCCCAAAGCTCCCACCTCCACTCG ATTCAGCGATGCCATCAGAGCGTTTCAGTGGGTGTCCCAGCTACCTGTCAGCGGCGTGTTGGA CCGCGCCACCTGCGCCAGATGACTCGTCCCCGCTGCGGGGTTACAGATACCAACAGTTATGC GGCCTGGGCTGAGAGGATCAGTGACTTGTTTGCTAGACACCGGACCAAAATGAGGCGTAAGAA ACGCTTTGCAAAGCAAGGTAACAAATGGTACAAGCAGCACCTCTCCTACCGCCTGGTGAACTG GCCTGAGCATCTGCCGGAGCCGGCAGTTCGGGGCGCCGTGCGCGCCCCTTCCAGTTGTGGAG CAACGTCTCAGCGCTGGAGTTCTGGGAGGCCCCAGCCACAGGCCCCGCTGACATCCGGCTCAC CTTCTTCCAAGGGGACCACAACGATGGGCTGGGCAATGCCTTTGATGGCCCAGGGGGCGCCCT GGCGCACGCCTTCCTGCCCCGCCGCCGCGAAGCGCACTTCGACCAAGATGAGCGCTGGTCCCT GAGCCGCCGCCGCGGCCCAACCTGTTCGTGGTGCTGGCGCACGAGATCGGTCACACGCTTGG CCTCACCCACTCGCCCGCGCGCGCGCGCTCATGGCGCCCTACTACAAGAGGCTGGGCCGCGA CGCGCTGCTCAGCTGGGACGACGTGCTGGCCGTGCAGAGCCTGTATGGGAAGCCCCTAGGGGG CTCAGTGGCCGTCCAGCTCCCAGGAAAGCTGTTCACTGACTTTGAGACCTGGGACTCCTACAG CACTGTAGACAGGCAACAGCAACTGTACATTTTTAAAGGGAGCCATTTCTGGGAGGTGGCAGC TGATGGCAACGTCTCAGAGCCCCGTCCACTGCAGGAAAGATGGGTCGGGCTGCCCCCAACAT TGAGGCTGCGGCAGTGTCATTGAATGATGGAGATTTCTACTTCTTCAAAGGGGGTCGATGCTG GAGGTTCCGGGGCCCCAAGCCAGTGTGGGGTCTCCCACAGCTGTGCCGGGCAGGGGGCCTGCC CCGCCATCCTGACGCCGCCTCTTCTTCCCTCCTCTGCGCCGCCTCATCCTCTTCAAGGGTGC CCGCTACTACGTGCTGGCCCGAGGGGGGACTGCAAGTGGAGCCCTACTACCCCCGAAGTCTGCA GGACTGGGGAGGCATCCCTGAGGAGGTCAGCGGCGCCCTGCCGAGGCCCGATGGCTCCATCAT CTTCTTCCGAGATGACCGCTACTGGCGCCTCGACCAGGCCAAACTGCAGGCAACCACCTCGGG CCGCTGGGCCACCGAGCTGCCTGGATGGGCTGCTGGCATGCCAACTCGGGGAGCGCCCTGTT C \underline{TGA} $\underline{AGGCACCTCCTCACCTCAGAAACTGGTGGTGCTCTCAGGGCAAAATCATGTTCCCCACC$ CCCGGGGCAGAACCCCTCTTAGAAGCCTCTGAGTCCCTCTGCAGAAGACCGGGCAGCAAAGCC

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FIGURE 144

MVARVGLLLRALQLLLWGHLDAQPAERGGQELRKEAEAFLEKYGYLNEQVPKAPTSTRFSDAI
RAFQWVSQLPVSGVLDRATLRQMTRPRCGVTDTNSYAAWAERISDLFARHRTKMRRKKRFAKQ
GNKWYKQHLSYRLVNWPEHLPEPAVRGAVRAAFQLWSNVSALEFWEAPATGPADIRLTFFQGD
HNDGLGNAFDGPGGALAHAFLPRRGEAHFDQDERWSLSRRRGRNLFVVLAHEIGHTLGLTHSP
APRALMAPYYKRLGRDALLSWDDVLAVQSLYGKPLGGSVAVQLPGKLFTDFETWDSYSPQGRR
PETQGPKYCHSSFDAITVDRQQQLYIFKGSHFWEVAADGNVSEPRPLQERWVGLPPNIEAAAV
SLNDGDFYFFKGGRCWRFRGPKPVWGLPQLCRAGGLPRHPDAALFFPPLRRLILFKGARYYVL
ARGGLQVEPYYPRSLQDWGGIPEEVSGALPRPDGSIIFFRDDRYWRLDQAKLQATTSGRWATE
LPWMGCWHANSGSALF

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation sites.

amino acids 164-168, 355-359

N-myristoylation sites.

amino acids 92-98, 153-159, 193-199, 202-208, 288-294, 368-374, 509-515

Amidation site.

amino acids 312-316

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 237-247

Matrixins cysteine switch

amino acids 231-262, 271-284

Hemopexin domain protein

amino acids 66-108, 231-262

FIGURE 145

GCCGGCTAGGGCGCCGGAGCCGCAGCCGCGGGGCTCCGAGAGGCGCGCACTGGGGCTGGGACTGCGCGGCG CGGCCCTCCGCGCAGCGTGGCTTCCGCTGCCCCCACGGAAGGCACGGGCTGGCGCTGCCGGGCGCCGGGGAGGAC GGCGAGGAGGAGGCGGCGGCGGAGACGGCGGCGGCGAGACTGGGGCCAGGGAGACAGCCCTGGGGGAGAGACGC AGCAGAGCCGCTGCCCTACTTCCTGCAGGAGCCACAGGACGCCTACATTGTGAAGAACAAGCCTGTGGAGCTCCG ACAGGAAGGCCTGGATGAGGCCACCGGCCTGCGGGTGCGCGAGGTGCAGATCGAGGTGTCGCGGCAGCAGGTGGA GGAGCTCTTTGGGCTGGAGGATTACTGGTGCCAGTGCGTGGCCTGGAGCTCCGCAGGCACCAACAAGAGTCGCCG AGCCTACGTCCGCATCGCCTACCTGCGCAAGAACTTCGATCAGGAGCCTCTGGGCAAGGAGGTGCCCCTGGACCA TGAGGTTCTCCTGCAGTGCCGCCGCCGGAGGGGGGGTGCCTGTGGCCGAGGTGGAATGGCTCAAGAATGAGGATGT CATCGACCCCACCCAGGACACCAACTTCCTGCTCACCATCGACCACAACCTCATCATCCGCCAGGCCCGCCTGTC GGACACTGCCAACTATACCTGCGTGGCCAAGAACATCGTGGCCAAACGCCGGAGCACCACTGCCACCGTCATCGT CTACGTGAATGGCGGCTGGTCCAGCTGGGCAGAGTGGTCACCCTGCTCCAACCGCTGTGGCCGAGGCTGGCAGAA GCGCACCCGGACCTGCACCAACCCCGCTCCACTCAACGGAGGGCCTTCTGCGAGGGCCAGGCATTCCAGAAGAC CGACTCTAAGAACTGCACAGATGGGCTGTGCATGCAAAATAAGAAAACTCTAAGCGACCCCAACAGCCACCTGCT GGAGGCCTCAGGGGATGCGGCGCTGTATGCGGGGGCTCGTGGTGGCCATCTTCGTGGTCGTGGCAATCCTCATGGC GGTGGGGGTGGTGTACCGCCGCAACTGCCGTGACTTCGACACAGACATCACTGACTCATCTGCTGCCCTGAC TGGTGGTTTCCACCCCGTCAACTTTAAGACGGCAAGGCCCAGCAACCCGCAGCTCCTACACCCCTCTGTGCCTCC TGACCTGACAGCCAGCGCGGCATCTACCGCGGACCCGTGTATGCCCTGCAGGACTCCACCGACAAAATCCCCAT GACCAACTCTCCTCTGCTGGACCCCTTACCCAGCCTTAAGGTCAAGGTCTACAGCTCCAGCACCACGGGCTCTGG ${\tt GCCAGGCCTGGCAGATGGGGCTGACCTGCTGGGGGTCTTGCCGCCTGGCACATACCCTAGCGATTTCGCCCGGGAATGGGGGTCTTGCCGCCTGGCACATACCCTAGCGATTTCGCCCGGGAATGGGGGTCTTGCCGCCTGGCACATACCCTAGCGATTTCGCCCGGGAATGGGGGTCTTGCCGCACATACCCTAGCGATTTCGCCCGGGAATGGGGGTCTTGCCGCCTGGCACATACCCTAGCGATTTCGCCCGGGAATGGGGGAATGGGGGATTTCGCCGGGAATGGGGGATTTCGCCGGGGAATGGGGGATTTCGCCGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGGAATGGGAATGGGGAATGGGAATGGGAATGGGAATGGGAATGGGAATGGGAATGGGAATGAATGA$ ${\tt CAATGGAGCCATTCCCCAGGGCAAGTTCTACGAGATGTATCTACTCATCAACAAGGCAGAAAGTACCCTCCCGCT}$ TTCAGAAGGGACCCAGACAGTATTGAGCCCCTCGGTGACCTGTGGACCCACAGGCCTCCTGCTGTGCCGCCCCGT CATCCTCACCATGCCCCACTGTGCCGAAGTCAGTGCCCGTGACTGGATCTTTCAGCTCAAGACCCAGGCCCACCA GGGCCACTGGGAGGAGGTGGTGACCCTGGATGAGGAGACCCTGAACACCCCTGCTACTGCCAGCTGGAGCCCAG GGCCTGTCACATCCTGCTGGACCAGCTGGGCACCTACGTGTTCACGGGCGAGTCCTATTCCCGCTCAGCAGTCAA GCGGCTCCAGCTGGCCGTCTTCGCCCCCGCCCTCTGCACCTCCCTGGAGTACAGCCTCCGGGTCTACTGCCTGGA GGACACGCCTGTAGCACTGAAGGAGGTGCTGGAGCTGGAGCCGGACTCTGGGCGGATACTTGGTGGAGGAGCCGAA CAAGCTGCTGGCCAAATACCAGGAGATCCCCTTCTATCACATTTGGAGTGGCAGCCAGAAGGCCCTCCACTGCAC GGGCCAGATATTCCAGCTGCATACCACTCTGGCAGAGACACCTGCTGGCTCCCTGGACACTCTCTGCCCCC TGGCAGCACTGTCACCACCCAGCTGGGACCTTATGCCTTCAAGATCCCACTGTCCATCCGCCAGAAGATATGCAA ${\tt CAGCCTAGATGCCCCCAACTCACGGGGCAATGACTGGCGGATGTTAGCACAGAAGCTCTCTATGGACCGGTACCT}$ GAATTACTTTGCCACCAAAGCGAGCCCCACGGGTGTGATCCTGGACCTCTGGGAAGCTCTGCAGCAGGACGATGG GGACCTCAACAGCCTGGCGAGTGCCTTGGAGGAGATGGGCAAGAGTGAGATGCTGGTGGCTGTGGCCACCGACGG TCCTGATGGGGATGTTTGGCCTCTGCTTCCTCCCAGTTCACAGCCAGAGTTGCCTCTCCTCCTCCTCCCCAA GGGCGGCAGGCAGGAGGCCCTCCCTCCACCCCCACCCTCAGCCCGGCAACTTCTGGGTTCCGTGGGTTTTAG ${\tt TTCCGTTCTTCGTTTTCTTCCTCCGTTATTGATTTCTCCTTTCTCCCTAAGCCCCCTTCTGCTTCCACGCCCTTT}$ TTTCTTAGGAAACGCAAACGATTTATTATCCAGATTATTTGGATAAGTCCTTTTTAAAA

FIGURE 146

MGARSGARGALLLALLCWDPRLSQAGTDSGSEVLPDSFPSAPAEPLPYFLQEPQDAYIVKNK PVELRCRAFPATQIYFKCNGEWVSQNDHVTQEGLDEATGLRVREVQIEVSRQQVEELFGLEDY WCQCVAWSSAGTTKSRRAYVRIAYLRKNFDQEPLGKEVPLDHEVLLQCRPPEGVPVAEVEWLK NEDVIDPTQDTNFLLTIDHNLIIRQARLSDTANYTCVAKNIVAKRRSTTATVIVYVNGGWSSW AEWSPCSNRCGRGWQKRTRTCTNPAPLNGGAFCEGQAFQKTACTTICPVDGAWTEWSKWSACS TECAHWRSRECMAPPPQNGGRDCSGTLLDSKNCTDGLCMQNKKTLSDPNSHLLEASGDAALYA GLVVAIFVVVAILMAVGVVVYRRNCRDFDTDITDSSAALTGGFHPVNFKTARPSNPQLLHPSV PPDLTASAGIYRGPVYALQDSTDKIPMTNSPLLDPLPSLKVKVYSSSTTGSGPGLADGADLLG VLPPGTYPSDFARDTHFLHLRSASLGSQQLLGLPRDPGSSVSGTFGCLGGRLSIPGTGVSLLV PNGAIPQGKFYEMYLLINKAESTLPLSEGTQTVLSPSVTCGPTGLLLCRPVILTMPHCAEVSA RDWIFQLKTQAHQGHWEEVVTLDEETLNTPCYCQLEPRACHILLDQLGTYVFTGESYSRSAVK RLQLAVFAPALCTSLEYSLRVYCLEDTPVALKEVLELERTLGGYLVEEPKPLMFKDSYHNLRL SLHDLPHAHWRSKLLAKYQEIPFYHIWSGSQKALHCTFTLERHSLASTELTCKICVRQVEGEG QIFQLHTTLAETPAGSLDTLCSAPGSTVTTQLGPYAFKIPLSIRQKICNSLDAPNSRGNDWRM LAQKLSMDRYLNYFATKASPTGVILDLWEALQQDDGDLNSLASALEEMGKSEMLVAVATDGDC

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 374-395

N-glycosylation sites.

amino acids 222-225, 347-350

Glycosaminoglycan attachment site.

amino acids 492-495

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 233-236, 234-237

Casein kinase II phosphorylation sites.

amino acids 30-33, 87-90, 251-254, 341-344, 359-362, 629-632, 651-654, 706-709, 757-760, 827-830, 925-928, 941-944

Tyrosine kinase phosphorylation sites.

amino acids 216-223, 773-780

N-myristoylation sites.

amino acids 2-7, 6-11, 27-32, 96-101, 137-142, 179-184, 247-252, 281-286, 334-339, 379-384, 491-496, 495-500, 509-514, 542-547, 547-552, 550-555, 553-558, 560-565, 611-616, 785-790, 834-839, 844-849

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 541-551

ATP/GTP-binding site motif A (P-loop).

amino acids 926-933

Growth factor and cytokines receptors family signature 2.

amino acids 306-312

FIGURE 147

GAGAGGGACAGAGGCTGGAGAAGGATGTATGGCCTGCCCTGGGCTTGTCTGTTCCCTCCTGAGCCTGAGCCCCTT ACCTTCCTGACCCC**ATG**AAGCACACACTGGCTCTGCTGGCTCCCCTGCTGGGCCTGGGGCCTGGGGCTGGCCCTGA GTCAGCTGGCTGCAGGGGCCACAGACTGCAAGTTCCTTGGCCCGGCAGAGCACCTGACATTCACCCCAGCAGCCA GGGCCCGGTGGCTGGCCCTCGAGTTCGTGCGCCAGGACTCCTGGACTCCCTCTATGGCACCGTGCGCCGCTTCC TCTCGGTGGTGCAGCTCAATCCTTTCCCTTCAGAGTTGGTAAAGGCCCTACTGAATGAGCTGGCCTCCGTGAAGG TGAATGAGGTGGTGCGGTACGAGGCGGGCTACGTGGTATGCGCTGTGATCGCGGGCCTCTACCTGCTGCTGGTGC CCACTGCCGGGCTTTGCTTCTGCTGCTGCCGCCGCCGCGCGCGCGGGGGACGAGTGAAGACAGAGCACAAGG CGCTGGCCTGTGAGCGCGCGCCCTCATGGTCTTCCTGCTGACCACCCTCTTGCTGCTGATTGGTGTGTCT GTGCCTTTGTCACCAACCAGCGCACGCATGAACAGATGGGCCCCAGCATCGAGGCCATGCCTGAGACCCTGCTCA GCCTCTGGGGCCTGGTCTCTGATGTCCCCCAAGAGCTGCAGGCCGTGGCACAACTTCTCCCTGCCCCAGGAGC AAGTCTCAGAGGAGCTGGATGGTGTTGGTGTGAGCATTGGGAGCGCGATCCACACTCAGCTCAGGAGCTCCGTGT CTACAGTGGTAGAGCTGCAGGCCGGGCAGCAGGACCTGGAGCCATCCGGGAACACCGGGACCGCCTCCTTG AGCTGCTGCAGGAGGCCAGGTGCCAGGGAGATTGTGCAGGGGCCCTGAGCTGGGCCCGCACCCTGGAGCTGGGTG GCATGGTCCAGGAGGAGAACAGCACCTTCAACGCCCTTCCAGCCCTGGCTGCCATGCAGACATCCAGCGTGGTGC AAGAGCTGAAGAAGGCAGTGGCCCAGCAGCCGGAAGGGGTGAGGACACTGGCTGAAGGGTTCCCGGGCTTGGAGG CAGCTTCCCGCTGGGCCCAGGCACTGCAGGAGGTGGAGGAGGCAGCCGCCCCTACCTGCAGGAGGTGCAGAGAT ACGAGACCTACAGGTGGATCGTGGGTGCTGCTGCTCCGTGGTCCTATTCGTGGTGCTCTGCAACCTGCTGG GCCTCAATCTGGGCATCTGGGGCCTGTCTGCCAGGGACGCCCAGCCACCCAGAAGCCAAGGGCGAGGCTGGAG $\verb|CCCGCTTCCTCATGGCAGGTGTGGGCCTCAGCTTCCTCTTTGCTGCACCCCTCATCCTCGTGTTTCGCCACCT|\\$ TCCTGGTGGGTGCCACGTGCAGACGCTGGTGTGCCGGAGCTGGGAGAACGGCGAGCTCTTTGAGTTTGCAGACA CCCCAGGGAACCTGCCCCGTCCATGAACCTGTCGCAACTTCTTGGCCTGAGGAAGAACATCAGCATCCACCAAG CCTATCAGCAGTGCAAGGAAGGGGCAGCGCTCTGGACAGTCCTGCAGCTCAACGACTCCTACGACCTGGAGGAGC ACCTGGATATCAACCAGTATACCAACAAGCTACGGCAGGAGTTGCAGAGCCTGAAAGTAGACACACAGAGCCTGG ${\tt ACTTCCTCGTTCAGATCCAGAGGCCCGTGGTGAAGACCAGCATGGAGCAGCTGGCCCAGGAGCTGCAAGGACTGG}$ CCCAGGCCCAAGACAATTCTGTGCTGGGGCAGCGGCTGCAGGAGGAGGCCCAAGGACTCAGAAACCTTCACCAGG AGAAGGTCGTCCCCAGCAGAGCCTTGTGGCAAAGCTCAACCTCAGCGTCAGGGCCCTGGAGTCCTCTGCCCCGA GGATCCTGAGGAATGTGAGTGAGTGTTTCCTGGCCCGGGAGATGGGCTACTTCTCCCAGTACGTGGCCTGGGTGA GAGAGGAGGTGACTCAGCGCATTGCCACCTGCCAGCCCCTCTCCGGAGCCCTGGACAACAGCCGTGTGATCCTGT GTGACATGATGCCTGACCCCTGGAATGCCTTCTGGTTCTGCCTGGCATGGTGCACCTTCTTCCTGATCCCCAGCA TCATCTTTGCCGTCAAGACCTCCAAATACTTCCGTCCTATCCGGAAACGCCTCAGCTCCACCAGCTCTGAGGAGA CTCAGCTCTTCCACATCCCCGGGTTACCTCCCTGAAGCTG<u>TAG</u>GGCCTTGTGGGGTGAGGTGACCCTGAGGCTG CCTGTCCTCCCCTTTGATTTAGCCTGGGCCACAGGACTTCGGTAGCTCTTGCCCCAGAGCCCAGGCTGGCATCCA GGCCTGGACTGTCCCCAGTTCCGGCTTACCTGGCCCCACCTTGCCTGCTCCTTTCCACCCCTTTCTGCTCACGAC $\tt CGTTACCCCCATGCTGGTGGCATCCTCACAGGAAGAGCCTGTTCTCCACCTGCTGGAGCCTGGACCCTGGGGTGG$ GACAGAGGCCTCGTCCAACCCCACTCCCCTTCCCGTGTGTCTTCCCCCTGCCAAGCCTCCCCTGCCAAGCCTCC $\verb|CCCTGCCCCTCTGGCCCCCCACACCGTCCTCATCTGGCCTCCCCCTGGCCCCCACTTCCCTCTT|\\$ ATGCCCTTCCTGGCCCTTTGCTTCCTCCCTTAGTCCCCTCTTCACCATATCTCCACTGCTACCTTGCTGGCCCCA CTGGCTGCAGGCCCTCCATGGCCTCTGAGCCCTCCACTGCCCCAGGGCCTTGGGCCCTCTGCAGATCTCATC ${\tt GGCCAGAACAGGATTTGCACGGCCCCTTTTATCCTGCGCATGTGGCCTAGGGTCATCCCCAGCCCATCCCTGTG}$

FIGURE 148

MKHTLALLAPLLGLGLGLALSQLAAGATDCKFLGPAEHLTFTPAARARWLAPRVRAPGLL
DSLYGTVRRFLSVVQLNPFPSELVKALLNELASVKVNEVVRYEAGYVVCAVIAGLYLLLV
PTAGLCFCCCRCHRRCGGRVKTEHKALACERAALMVFLLLTTLLLLIGVVCAFVTNQRTH
EQMGPSIEAMPETLLSLWGLVSDVPQELQAVAQQFSLPQEQVSEELDGVGVSIGSAIHTQ
LRSSVYPLLAAVGSLGQVLQVSVHHLQTLNATVVELQAGQQDLEPAIREHRDRLLELLQE
ARCQGDCAGALSWARTLELGADFSQVPSVDHVLHQLKGVPEANFSSMVQEENSTFNALPA
LAAMQTSSVVQELKKAVAQQPEGVRTLAEGFPGLEAASRWAQALQEVEESSRPYLQEVQR
YETYRWIVGCVLCSVVLFVVLCNLLGLNLGIWGLSARDDPSHPEAKGEAGARTLMAGVGL
SFLFAAPLILLVFATFLVGGNVQTLVCRSWENGELFEFADTPGNLPPSMNLSQLLGLRKN
ISIHQAYQQCKEGAALWTVLQLNDSYDLEEHLDINQYTNKLRQELQSLKVDTQSLDLLSS
AARRDLEALQSSGLQRIHYPDFLVQIQRPVVKTSMEQLAQELQGLAQAQDNSVLGQRLQE
EAQGLRNLHQEKVVPQQSLVAKLNLSVRALESSAPNLQLETSDVLANVTYLKGELPAWAA
RILRNVSECFLAREMGYFSQYVAWVREEVTQRIATCQPLSGALDNSRVILCDMMADPWNA
FWFCLAWCTFFLIPSIIFAVKTSKYFRPIRKRLSSTSSEETQLFHIPRVTSLKL

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 105-125, 153-173, 428-449, 476-500, 778-797

N-glycosylation sites:

amino acids 270-273, 343-347, 352-356, 530-534, 540-546, 563-567, 684-688, 707-711, 725-729

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 811-815

Tyrosine kinase phosphorylation site.

amino acids 95-103

N-myristoylation sites.

amino acids 13-19, 15-21, 17-23, 26-32, 58-64, 124-130, 168-174, 228-234, 230-236, 320-326, 338-344, 393-399, 429-435, 446-452, 477-483, 500-506, 536-542, 644-650, 761-767

Phospholipase A2 histidine active site.

aminop acids 129-137

4Fe-4S ferredoxins, iron-sulfur binding region signature.

amino acids 126-138

Mitochondrial energy transfer proteins signature.

amino acids 80-89

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FIGURE 149

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FIGURE 150

 ${\tt MRLLVLSSLLCILLLCFSIFSTEGKRRPAKAWSGRRTRLCCHRVPSPNSTNLKGHHVRLCKPC} \\ {\tt KLEPEPRLWVVPGALPQV}$

Important features of the protein:

Signal peptide:

amino acids 1-21

N-glycosylation site.

amino acids 48-52

Amidation sites.

amino acids 23-27, 33-37

FIGURE 151

CACCGGAGGGCACCCGACCTGACGGAGCTGCGCTGCGTTCGCCTCGTTTGCCTCGCGCCCTCCA CTGGAGCTGTTCGCGCCTCCCGGCTCCCACCGCAGCCCACCCGGCAGAGGAGTCGCTACCAGC GCCCAGTGCGCTCTGTCAGTCCGCAAACTCCTTGCCGCCCCGGGCCCGGGCTGGGCACCAAATAC CAGGCTACC**ATG**GTCTACAAGACTCTCTTCGCTCTTTGCATCTTAACTGCAGGATGGAGGGTA CAGAGTCTGCCTACATCAGCTCCTTTGTCTGTTTCTCTTCCGACAAACATTGTACCACCGACC ACCATCTGGACTAGCTCTCCACAAAACACTGATGCAGACACTGCCTCCCCATCCAACGGCACT CACAACAACTCGGTGCTCCCAGTTACAGCATCAGCCCCAACATCTCTGCTTCCTAAGAACATT TCCATAGAGTCCAGAGAAGAGGGAGATCACCAGCCCAGGTTCGAATTGGGAAGGCACAAACACA GACCCCTCACCTTCTGGGTTCTCGTCAACAAGCGGTGGAGTCCACTTAACAACCACGTTGGAG GAACACAGCTCGGGCACTCCTGAAGCAGGCGTGGCAGCTACACTGTCGCAGTCCGCTGCTGAG CCTCCCACACTCATCTCCCCTCAAGCTCCAGCCTCATCACCCTCATCCCTATCAACCTCACCA CCTGAGGTCTTTTCTGCCTCCGTTACTACCAACCATAGCTCCACTGTGACCAGCCCCAACCC ACTGGAGCTCCAACTGCACCAGAGTCCCCGACAGAGGAGTCCAGCTCTGACCACACACCCCACT TCACATGCCACAGCTGAGCCAGTGCCCCAGGAGAAACACCCCCAACAACTGTGTCAGGCAAA GTGATGTGTGAGCTCATAGACATGGAGACCACCACCACCTTTCCCAGGGTGATCATGCAGGAA GTAGAACATGCATTAAGTTCAGGCAGCATCGCCGCCATTACCGTGACAGTCATTGCCGTGGTG CTGCTGGTGTTTGGAGTTGCAGCCTACCTAAAAATCAGGCATTCCTCCTATGGAAGACTTTTG GACGACCATGACTACGGGTCCTGGGGAAACTACAACAACCCTCTGTACGATGACTCC**TAA**CAA TGGAATATGGCCTGGGATGAGGATTAACTGTTCTTTATTATAAGTGCTTATCCAGTAGAATT AATAAGTACCTGATGCGCATTGAACGACAATCTTAAGCCCTGTTTTGTTGGTATGGTTGTTTT TGTTTTCCTCCTCTCTCTGGCTGCTACAACTTCCCCTTTCTGGTACAAGAAGAACCATTCT ATTTGGGTTGTTTTGTTAGGGGTTACTTTCAGGGGAACATTTCATTTGTGTTATTTCTTAAAC TTCTATTTAGGAAATTACATTAAGTATTAATGAGGGGAAAGGAAATGAGCTCTACGAGGATTT CACCTTGCATGGGAGAGAGCAGGGTTTTCTCAGATTCCTTTTTAATCTCTATTTATCTGGTTG TTTCTGACAGGATGCTGCCTTGGCTCTACGAGCTGGAAAGCAGCTTCTTAGCTGCCTAAT TAATGAAAGATGAAAATAGGAAGTGCCCTGGAGGGGGCCAGCAGGTCACGGGGCAGAATCTCT CAGGTTGCTGTGGGATCTCAGTGTGCCCCTACCTGTTCTCCCCTCCAGGCCACCTGTCTCTGT AAAGGATGTCTGCTCTGTTCAAAAGGCAGCTGGGATCCCAGCCCACAAGTGATCAGCAGAGTT GCATTTCCAAAGAAAAGGCTATGAGATGAGCTGAGTTATAGAGAGAAAGGGAGAGGCATGTA CGGTGTGGGGAAGTGGAAGAGCTGGCGGGGGAGAAGGAGGCTAACCTGCACTGAGTACTT CATTAGGACAAGTGAGAATCAGCTATTGATAATGGCCAGAGATATCCACAGCTTGGAGGAGCC TGGCTGTAAAATGTTTAAAAAC

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FIGURE 152

MVYKTLFALCILTAGWRVQSLPTSAPLSVSLPTNIVPPTTIWTSSPQNTDADTASPSNGTHNN SVLPVTASAPTSLLPKNISIESREEEITSPGSNWEGTNTDPSPSGFSSTSGGVHLTTTLEEHS SGTPEAGVAATLSQSAAEPPTLISPQAPASSPSSLSTSPPEVFSASVTTNHSSTVTSTQPTGA PTAPESPTEESSSDHTPTSHATAEPVPQEKTPPTTVSGKVMCELIDMETTTTFPRVIMQEVEH ALSSGSIAAITVTVIAVVLLVFGVAAYLKIRHSSYGRLLDDHDYGSWGNYNNPLYDDS

Important features of the protein:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 258-278

N-glycosylation sites.

amino acids 58-61, 62-65, 80-83, 176-179

Casein kinase II phosphorylation sites.

amino acids 49-52, 85-88, 95-98, 100-103, 120-123, 121-124, 141-144, 164-167, 191-194, 195-198, 200-203

Tyrosine kinase phosphorylation site.

amino acids 289-296

N-myristoylation sites.

amino acids 59-64, 115-120, 128-133, 133-138, 257-262, 297-302

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FIGURE 153

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FIGURE 154

MLVHCVGLLLTGLLLGAGALLASEPIYQPPSAWVPAGGLVGLALLGALLTLRWPRPFTV LGTTLLGSAVLVACVDYFLEGLALGSWLGQRLQTLPALPSLC

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 38-55, 60-78

N-myristoylation sites.

amino acids 7-13, 12-18, 16-22, 22-28, 41-47, 50-56, 84-90, 88-94

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 67-78

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FIGURE 155

TGCAATTAAAGGAGTCGGGTCTCTAACTGTTGATCTGTTTTTTTCCCTTCTGAGCA**ATG**GAGC TTACCATCTTTATCCTGAGACTGGCCATTTACATCCTGACATTTCCCTTGTACCTGCTGAACT TTCTGGGCTTGTGGAGCTGGATATGCAAAAAATGGTTCCCCTACTTCTTGGTGAGGTTCACTG TGATATACAACGAACAGATGGCAAGCAAGAAGCGGGAGCTCTTCAGTAACCTGCAGGAGTTTG CGGGCCCCTCCGGGAAACTCTCCCTGCTGGAAGTGGGCTGTGGCACGGGGGCCAACTTCAAGT TCTACCCACCTGGGTGCAGGGTGACCTGTATTGACCCCAACCCCAACTTTGAGAAGTTTTTGA TCAAGAGCATTGCAGAGAACCGACACCTGCAGTTTGAGCGCTTTGTGGTAGCTGCCGGGGAGA ACATGCACCAGGTGGCTGATGGCTCTGTGGATGTGGTGGTCTGCACCCTGGTGCTGTGCTCTG TGAAGAACCAGGAGCGGATTCTCCGCGAGGTGTGCAGAGTGCTGAGACCGGGAGGGGCTTTCT ATTTCATGGAGCATGTGGCAGCTGAGTGTTCGACTTGGAATTACTTCTGGCAACAAGTCCTGG AGCGGGCCAGCTTCTCTAAGCTGAAGCTGCAGCACATCCAGGCCCCACTGTCCTGGGAGTTGG TGCGCCCTCATATCTATGGATATGCTGTGAAA**TAG**TGTGAGCTGGCAGTTAAGAGCTGAATGG CTCAAAGAATTTAAAGCTTCAGTTTTACATTTAAAATGCTAAGTGGGAGAAGAGAAACCTTTT TTGAACCCAGAAGGCGAAGGTTGCAGTGAACCGAGATCATGCCATTGTACTCTAGCCTGGGTG GGGGTCTCACTGTGTTGCCTAGGCCGGTCTTGAACTCCTGGGCTCAAGTGATTCTCCCACCTT GACCTCCTAAATTGTTGGGATTACAGGTGTGAGACAGTGCACCTGGCCGAAATAGCTCAAGTT TCTGAAAAACAAATCTGAATCTATTTGTTATTCTTAGCGTCACTGGTCTGGCTTTCAGAATTA ACATACAAGGTTGCCACACCTAGTTCTGCCCAGCTTTATGTCTTTTATTCCAGTATTCCACCA AAGTTTGTTTTCCTGCATTCCAGTTCTCAAGTCTTAAGATAAAGATTGTACTTGACAGTTTAG TATATCCATAAAACTATTTGAGGTGGTTAAGGTTCTTGGGTTCATTTTCCTTAATACTTTGCT GAATATTGTAGATTGTAGGCAATGAAAAAGTCTACTAAATTAGGAAAACCTTGAATAATTAGG TTGGATTATTCTTATCTAATTCCACCCCTGTTGGAAGATGATTTCTTTGTTCTTTGCAACTAT ATATTTTCTGCAATGGTTTGTAGGAATTTTAATAAATGTAGTATATTTTCTGAGATGATTTTG TAAAAGTACTATTTTAAATATCAAATCAACCAATAAATTCACATTTGTGTTAGGAACAAAA

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FIGURE 156

MELTIFILRLAIYILTFPLYLLNFLGLWSWICKKWFPYFLVRFTVIYNEQMASKKRELFSNLQ EFAGPSGKLSLLEVGCGTGANFKFYPPGCRVTCIDPNPNFEKFLIKSIAENRHLQFERFVVAA GENMHQVADGSVDVVVCTLVLCSVKNQERILREVCRVLRPGGAFYFMEHVAAECSTWNYFWQQ VLDPAWHLLFDGCNLTRESWKALERASFSKLKLQHIQAPLSWELVRPHIYGYAVK

Signal peptide:

amino acids 1-29

N-glycosylation site.

amino acids 203-207

N-myristoylation sites.

amino acids 78-84, 80-86, 91-97, 201-207

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FIGURE 157

CCGCTGAGATGTACGAACTTCCGGTTCTCCGGGCAGCTGCCACTGCTGTAGCTTCTGCCACCT GCCACGACCGGGCCTCTCCCTGGCGTTTGGTCACCTCTGCTTCATTCTCCACCGCGCCTATGG TCCCTCTTGGAGCCAGCGTGGCGGCCTGGCGGCTCCCGGGTGGTGAGAGAGCGGTCCGGGAA CG**ATG**AAGGCCTCGCAGTGCTGCTGCTGTCTCAGCCACCTCTTGGCTTCCGTCCTCCTGC GTCTTGGGCCTCCTGACCCTAGACCACGGACATTACCGCCGCTGCCACCGGGCCCTACCCCTG GCAGCAACCCTGTGGCCGGGCTTGAGACGGACGATCACGGAGGGAAGGCCGGGGAAGGCTCGG TGGGTGGCGGCCTTGCTGTGAGCCCCAACCCTGGCGACAAGCCCATGACCCAGCGGGCCCTGA CCGTGTTGATGGTGAGCGGCGCGGTGCTGGTGTACTTCGTGGTCAGGACGGTCAGGATGA GAAGAAGAACCGAAAGACTAGGAGATATGGAGTTTTGGACACTAACATAGAAAATATGGAAT TGACACCTTTAGAACAGGATGATGAGGATGATGACAACACGTTGTTTGATGCCAATCATCCTC GAAGA**TAA**GAATGTGCCTTTTGATGAAAGAACTTTATCTTTCTACAATGAAGAGTGGAATTTC TAACAACCTTTAATTTGCTGTTGCAATAAATACCGTATCCTTTTATTATATCTTTATATGTAT AGAAGTACTCTATTAATGGGCTCAGAGATGTTGGGGGATAAAGTATACTGTAATAATTTATCTG TTTGAAAATTACTATAAAACGGTGTTTTCTGGTCGGTTTTTTGTTTCCTGCTTACCATATGATT GTAAATTGTTTTATGTATTAATCAGTTAATGCTAATTATTTTTTGCTGATGTCATATGTTAAAG AGCTATAAATTCCAACAACCAACTGGTGTGTAAAAATAATTTAAAATTTCCTTTACTGAAAGG TATTTCCCATTTTTGTGGGGAAAAGAAGCCAAATTTATTACTTTGTGTTGGGGTTTTTAAAAT AAAAA

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FIGURE 158

MKASQCCCCLSHLLASVLLLLLLPELSGPLAVLLQAAEAAPGLGPPDPRPRTLPPLPPGPTPA QQPGRGLAEAAGPRGSEGGNGSNPVAGLETDDHGGKAGEGSVGGGLAVSPNPGDKPMTQRALT VLMVVSGAVLVYFVVRTVRMRRRNRKTRRYGVLDTNIENMELTPLEQDDEDDDNTLFDANHPRR

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 124-140

N-glycosylation site.

amino acids 83-87

N-myristoylation sites.

amino acids 69-75, 78-84, 81-87, 97-103, 103-109, 106-112, 157-160

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FIGURE 159

GCTGCAGGCGGCGACGGCTACACC**ATG**GGCCGGCTGCTGCGGGCCGCCCGGCTGCCGCCGCTG GATGAGCCTGGCCCAGAGGGCCTCACCTCCACCTCCTGCTAGACCTCCTGCTGCCCACTGGC TTGGAGCCACTGGACTCAGAGGAGCCTAGTGAGACCATGGGCCTGGGAGCTGGGCTGGGAGCC TCTGGCTCAGGCTTCCCCAGCGAAGAGAATGAAGAGTCTCGGATTCTGCAGCCACCACAGTAC TTCTGGGAAGAGGGAGGAGGCTGAATGACTCAAGTCTGGACCTGGGACCCACTGCAGATTAT GTTTTTCCTGACTTAACTGAGAAGGCAGGTTCCATTGAAGACACTAGCCAGGCTCAAGAGCTG CCAAACCTCCCCTCTCCCTTGCCCAAGATGAATCTGGTTGAGCCTCCCTGGCATATGCCTCCC GAGGAGGAGGAGGAGGAGCTGCTCCCTGTGAATGGATCCCAAGAAGAAGCCAAGCCTCAG GTCCGTGACTTTTCTCTCACCAGCAGCAGCCAGACCCCAGGGGCCACCAAAAGCAGGCATGAA GACTCCGGGGACCAGGCCTCATCAGGTGTGGAGGTGGAGCAGCATGGGGCCCCAGCTTGCTG CTGCCTTCAGTCACCCCAACTACAGTGACTCCGGGGGACCAGGACTCCACCAGCCAAGAGGCA GAGGAAGCCACTGCAGGAGCAGCTGGTTTGTCTGGCCAGCACGAGGAGGTGCCGGCCTTGCCT TCATTCCCTCAAACCACAGCTCCCAGTGGGGCCGAGCACCCAGATGAAGATCCCCTTGGCTCT AGAACCTCAGCCTCTTCCCCACTGGCCCCTGGAGACATGGAACTGACACCTTCCTCTGCTACC TTGGGACAAGAAGATCTCAACCAGCAGCTCCTAGAAGGGCAGCAGCTGAAGCTCAATCCAGG ATCATTCTGAACATGACAGAGAACATAGACTGTGAGGTGTTCCGGCAGCACCGGGGGCCCACAG CTCCTGGCCCTGGTGGAAGAGGTGCTGCCCCGCCATGGCAGTGGCCACCATGGGGCCTGGCAC ATCTCTCTGAGCAAGCCCAGCGAGAAGGAGCAGCACCTTCTCATGACACTGGTGGGCGAGCAG GGGGTGGTGCCCACTCAAGATGTCCTTTCCATGCTGGGTGACATCCGCAGGAGCCTGGAGGAG GACTACGGCACGCTCTTCGTGGTGCTGGTGGTCATTGGGGCCCATCTGCATCATCATCATTGCG CTTGGCCTGCTCTACAACTGCTGGCAGCGCCGGCTGCCCAAGCTCAAGCACGTGTCGCACGGC GAGGAGCTGCGCTTCGTGGAGAACGGCTGCCACGACAACCCCACGCTGGACGTGGCCAGCGAC AGCCAGTCGGAGATGCAGGAGAAGCACCCCAGCCTGAACGGCGGGGGCCCTCAACGGCCCG GGGAGCTGGGGGGCGCTCATGGGGGGCCAAGCGGGACCCCGAGGACTCGGACGTGTTCGAGGAG GACACGCACCTG<u>TGAGCGCAGCCGAGGCGCAGGCCGAGTGGGCCGCCAGGACCAAGCGAGGTG</u> GACCCGAAACGGACGCCCGGAGCCCGCACCAGCCCGCGCCTACCCGGGCCGCCCCCGCGG CCTGGCCCTCGGCGCGGCTCCTTCCCGCTTCCCCCGACTTCACACGGCGGCTTCGGACCAAC TCCCTCACTCCCGCCCGAGGGGCAGGCCTCAAAGCCCGCCTTGGCCCCGCTTTCCCGCCCCTG AACCCCGGCCCGCGGGCGGCGGCGCGCTTCCTGCGCCCCGGGACTCAATTAAACCCGCCC GGAGACCACGCCGGGCCCAGCAAAA

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FIGURE 160

MGRLLRAARLPPLLSPLLLLLVGGAFLGACVAGSDEPGPEGLTSTSLLDLLLPTGLEPLDSEE
PSETMGLGAGLGASGSGFPSEENEESRILQPPQYFWEEEEELNDSSLDLGPTADYVFPDLTEK
AGSIEDTSQAQELPNLPSPLPKMNLVEPPWHMPPREEEEEEEEEEEEEEEEEL
LPVNGSQEEAKPQVRDFSLTSSSQTPGATKSRHEDSGDQASSGVEVESSMGPSLLLPSVTPTT
VTPGDQDSTSQEAEATVLPAAGLGVEFEAPQEASEEATAGAAGLSGQHEEVPALPSFPQTTAP
SGAEHPDEDPLGSRTSASSPLAPGDMELTPSSATLGQEDLNQQLLEGQAAEAQSRIPWDSTQV
ICKDWSNLAGKNYIILNMTENIDCEVFRQHRGPQLLALVEEVLPRHGSGHHGAWHISLSKPSE
KEQHLLMTLVGEQGVVPTQDVLSMLGDIRRSLEEIGIQNYSTTSSCQARASQVRSDYGTLFVV
LVVIGAICIIIIALGLLYNCWQRRLPKLKHVSHGEELRFVENGCHDNPTLDVASDSQSEMQEK
HPSLNGGGALNGPGSWGALMGGKRDPEDSDVFEEDTHL

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 499-521

N-glycosylation sites.

amino acids 106-110, 193-197, 395-399, 480-484

Glycosaminoglycan attachment site.

amino acids 77-81

N-myristoylation sites.

amino acids 24-30, 28-34, 41-47, 69-75, 71-77, 73-79, 75-81, 216-222, 327-333, 455-461, 519-525, 574-580, 581-587, 584-590

Amidation site.

amino acids 588-592

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FIGURE 161

CCAGGGCGGAGCGCAGCTGCGCCGGGCTTGGGCCCTGGGGCCGCCGCTCCCCACCGTCGTTT CTGCTAGGGGTTCTGCTGGGTGCGGCGCGCCTGCCGCGGGGCAGAAGCTTTTGAGATT GCTCTGCCACGAGAAAGCAACATTACAGTTCTCATAAAGCTGGGGACCCCGACTCTGCTGGCA AAACCCTGTTACATCGTCATTTCTAAAAGACATATAACCATGTTGTCCATCAAGTCTGGAGAA AGAATAGTCTTTACCTTTAGCTGCCAGAGTCCTGAGAATCACTTTGTCATAGAGATCCAGAAA AATATTGACTGTATGTCAGGCCCATGTCCTTTTGGGGAGGTTCAGCCTTCAGCCCTCGACATCG TTGTTGCCTACCCTCAACAGAACTTTCATCTGGGATGTCAAAGCTCATAAGAGCATCGGTTTA GAGCTGCAGTTTTCCATCCCTCGCCTGAGGCAGATCGGTCCGGGTGAGAGCTGCCCAGACGGA GTCACTCACTCAGCGGCCGAATCGATGCCACCGTGGTCAGGATCGGAACCTTCTGCAGC AATGGCACTGTGTCCCGGATCAAGATGCAAGAAGGAGTGAAAATGGCCTTACACCTCCCATGG TTCCACCCCAGAAATGTCTCCGGCTTCAGCATTGCAAACCGCTCATCTATAAAACGTCTGTGC ATCATCGAGTCTGTGTTTGAGGGTGAAGGCTCAGCAACCCTGATGTCTGCCAACTACCCAGAA GGCTTCCCTGAGGATGAGCTCATGACGTGGCAGTTTGTCGTTCCTGCACACCTGCGGGCCAGC GTCTCCTTCCTCAACTTCAACCTCTCCAACTGTGAGAGGAGGAGGAGGGGGTTGAATACTAC ATCCCGGGCTCCACCACCAACCCCGAGGTGTTCAAGCTGGAGGACAAGCAGCCTGGGAACATG GCGGGGAACTTCAACCTCTCTCTGCAAGGCTGTGACCAAGATGCCCAAAGTCCAGGGATCCTC CGGCTGCAGTTCCAAGTTTTGGTCCAACATCCACAAAATGAAAGCAGTGAG**TGA**GCCCCACTT TCCTTTTTCTTCCTCCAGCACCTTCGTTGTTTCCTGGGTAGTCTGCCTGGGTGAGGCTCC CTTCCTGTTTCTCATCTGTGGCTTCTGAAACACTTAGACTCTGGACCCAGCAAGAGTTTCAGG AAGTGGGTTGCTAGGCAGTTAGACAGGCTTGTTGGTGAACACCCGGTATGTAGTTCCATTTCA GCACAATAAAAGAAATCTTGCATTCAAGATGCTAAATTGTTTTTAACGAAAA

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FIGURE 162

MAGLNCGVSIALLGVLLLGAARLPRGAEAFEIALPRESNITVLIKLGTPTLLAKPCYIVISKR
HITMLSIKSGERIVFTFSCQSPENHFVIEIQKNIDCMSGPCPFGEVQLQPSTSLLPTLNRTFI
WDVKAHKSIGLELQFSIPRLRQIGPGESCPDGVTHSISGRIDATVVRIGTFCSNGTVSRIKMQ
EGVKMALHLPWFHPRNVSGFSIANRSSIKRLCIIESVFEGEGSATLMSANYPEGFPEDELMTW
QFVVPAHLRASVSFLNFNLSNCERKEERVEYYIPGSTTNPEVFKLEDKQPGNMAGNFNLSLQG
CDQDAQSPGILRLQFQVLVQHPQNESSE

Signal peptide:

amino acids 1-29

N-glycosylation sites.

amino acids 39-43, 122-126, 180-184, 205-209, 213-217, 270-274, 310-314, 339-343

Tyrosine kinase phosphorylation site.

amino acids 276-284

N-myristoylation sites.

amino acids 3-9, 7-13, 158-164, 175-181, 191-197, 303-309

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FIGURE 163

CAACCACACCTGGGGAATTGCTGGCCTGACTTCTGACCCCTGACTCCTCATACCCTTCCTC CAGAGCATGACATTTGACCACCAACTGAAACCTGACCTCTGACCCCAGACCACTGGCCCTTCC ${\tt CCCGCCCTGTGGTGACTTCATAAAGGTTACTAGCTTCTCCCCTGGCCTTGAGACCCACACG{\tt AT}}$ **G**GCCCTGCTGGCCAGTGCCGTCCCCTCTGCCCTGCTGGCCTGGCTGTCTTCAGGGT GCCCGCCTGGGCCTGTCTCCTCTGCTTCACAACCTACTCTGAGCGCCTCCGCATCTGCCAGAT GTTTGTTGGGATGCGGAGCCCCAAGCTTGAAGAGTGTGAGGAGGCCTTCACGGCCGCCTTCCA GGGCCTCTCTGACACCGAAATCAGTGAGGAGACCATCCACACTTCATCAGTGTCCTGGGGAAG CAGAGGAGAAAGGCTCAAAGACCATGAGAACAACAGAGACTTAGGGACAGAGAGACACAGACA GGGGAAGACAGCAGGGCAAAGACTCAGAGAGGGGAGGATGGAGAGTCAGAGAGGGGAAGATGG GATGGAGACTCAGGAGTATGGAGAGTCAGAGAGGGGAGGATGGACACTCAGGGGAGGATGGAG AGTCAGGAGGATGGAGACTCATAGAAAGGGGAGGATGGAGAGTCAGGAGAGGTTGGAGACTGG AGAGGGAATAGAGACCCAGAAAGGGGAGGATGGAGACTCAGAGGGTGGAAGATGGAGACTCAA AGAGGATGGAAACCCAGAGAGAGGAGGACAGAGACAGAGACTAGGGGAAGCAGGATAG CGACTGGTCGGGGGCAGAGACTCAGGGAGGATAGAGACTCACAGAGAGGTGAGGATAGAGACT TGGGAGGGACTCAGGAAGCATAGCGACTGTGGGGCAAAGAGTCAGAGAGGGGAGGATACAGAC TTGGGAGGGCAGAGACTCAGAAACAGAATGTTCGCATTAGGGACATGGTGTTGCGGGGAGCTG CCTCCCCAGCCCCTGCTCCCTCACCGCCAGACTATGATGAGAGAAGCCACCTGCATGA TGCCTTCCCTGATGCTGCAGAGAAAATGAAGAAGGTCATTACACAGCTTAAAGAAGCCCAGGC TTGCATCCCTCCCTGCGGTCTCCAGGAGTTCGCCCGGCGTTTCCTCTGCAGCGGGTGCTACTC TAGGGTCTGCGACCTCCCGCTGGACTGCCCAGTTCAGGATGTGACAGTGACTCGGGGCGACCA GGCTATGTTTTCTTGCATCGTAAACTTCCAGCTGCCAAAGGAGGAGATCACCTATTCCTGGAA GTTCGCAGGAGGAGGTCTCCGGACTCAGGACTTGTCCTATTTCCGAGATATGCCGCGGGCCGA AGGATACCTGGCGCGGATCCGGCCGGCTCAGCTCACGCACCGCGGGACGTTCTCCTGCGTGAT ATCAGCGAGTGCGACAGTGTTGGCGTGGTGAGTTCTGGGGACTCCGGAGCCCCAGCATCTAGC TCCCCGCTGTCTCAGATCCCACCGAGAAGTCTGGGTTCCCAGCAACCTCCAACCCAGGAGGAT GTTCTTTCGATGGTACTGCAGTGGCAACTAACAAAGGTATCTTTCCTCCTTCCCTATCCTATT AAAAAAAAAAAA

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FIGURE 164

MALLALASAVPSALLALAVFRVPAWACLLCFTTYSERLRICQMFVGMRSPKLEECEEAFTAAF QGLSDTEISEETIHTSSVSWGRCRGRAGEAQRVRLRDRQRETVRGERLKDHENNRDLGTERHR QGKTAGQRLREGRMESQRGEDGDSERGEDGDSEREEDGDSEGKMETQEYGESERGGWTLRGGW RVRRMETHRKGRMESQERLETGEGIETQKGEDGDSEGGRWRLKEDGNPERGGQR

Signal peptide:

amino acids 1-26

N-myristoylation site.

amino acids 65-71

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FIGURE 165

CAGAATCGCAGATTGCCAGCCCTTTTCCCGACCCCTACGGAAAGACGAGTCCAGGGGCCGTCC TGGCGAGGTCAAAACATTTAGTCTGGTCTTTTCAGCGTGGACCCTGCCAGCAGCCAGGCC**ATG** GAGCTCTCTGATGTCACCCTCATTGAGGGTGTGGGTAATGAGGTGATGGTGGTGGCAGGTGTG AACCAGCTCCTGGGCGCTATTGTGTCAGCAGGCGACACATCCGTCCTCCACCTGGGGCATGTG AATGATGAGAAGGCTGAAGAGGCGGGTGAAGGTCGGGGAGACTCCACTGGGGAGGCTGGAGCT GGGGGTGGTGTTGAGCCCAGCCTTGAGCATCTCCTTGACATCCAAGGCCTGCCCAAAAGACAA GCAGGTGCAGCAGCAGCAGTCCAGAGGCCCCCTGAGATCTGAGGATAGCACCTGCCTCCCT GCTAGGCCAGAGGATACCGTGGGTGCCCTGAAGAGCAAATACTTCCCTGGACAAGAAAGCCAG ATGAAACTGATCTACCAGGGCCGCCTGCTACAAGACCCAGCCCGCACACTGCGTTCTCTGAAC ATTACCGACAACTGTGTGATTCACTGCCACCGCTCACCCCCAGGGTCAGCTGTTCCAGGCCCC TCAGCCTCCTTGGCCCCCTCGGCCACTGAGCCACCCAGCCTTGGTGTCAATGTGGGCAGCCTC ATGGTGCCTGTCTTTGTGGTGCTGTTGGGTGTGTGTACTTCCGAATCAATTACCGCCAA TTCTTCACAGCACCTGCCACTGTCTCCCTGGTGGGAGTCACCGTCTTCTTCAGCTTCCTAGTA TTTGGGATGTATGGACGA**TAA**GGACATAGGAAGAAATGAAAGGCATGGTCTTTCTCCTTTAT TGTGATGGAAATCTCCTCCATAGGACACAGGAGGCAAGTATGCGGCCTCCCCTTCTCATCCAC AGGAGTACAGATGTCCCTCCCGTGCGAGCACACTCAGGTAGAAATGAGGATGTCATCTTCCT TCACTTTTAGGGTCCTCTGAAGGAGTTCAAAGCTGCTGGCCAAGCTCAGTGGGGAGCCTGGGC TCTGAGATTCCCTCCCACCTGTGGTTCTGACTCTTCCCAGTGTCCTGCATGTCTGCCCCCAGC ACCCAGGGCTGCCTGCAAGGGCAGCTCAGCATGGCCCCAGCACAACTCCGTAGGGAGCCTGGA GTATCCTTCCATTTCTCAGCCAAATACTCATCTTTTGAGACTGAAATCACACTGGCGGGAATG AAGATTGTGCCAGCCTTCTCTTATGGGCACCTAGCCGCCTTCACCTTCTTCCTCTACCCCTTA AGAGTCCTTCATAGAGCTCAGTCAGGAAGGGGATGGGGCACCAAGCCAAGCCCCAGCATTGG GAGCGGCCAGGCCACAGCTGCTGCTCCCGTAGTCCTCAGGCTGTAAGCAAGAGACAGCACTGG CCCTTGGCCAGCGTCCTACCCTGCCCAACTCCAAGGACTGGGTATGGATCGCTGGGCCCTAGG CTCTTGCTTCTGGGGCTATTGGAGGGTCAGTGTCTGTGACTGAATAAAGTTCCATTTTGTGGA

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FIGURE 166

MELSDVTLIEGVGNEVMVVAGVVVLILALVLAWLSTYVADSGSNQLLGAIVSAGDTSVLHLGH VDHLVAGQGNPEPTELPHPSEGNDEKAEEAGEGRGDSTGEAGAGGGVEPSLEHLLDIQGLPKR QAGAGSSSPEAPLRSEDSTCLPPSPGLITVRLKFLNDTEELAVARPEDTVGALKSKYFPGQES QMKLIYQGRLLQDPARTLRSLNITDNCVIHCHRSPPGSAVPGPSASLAPSATEPPSLGVNVGS LMVPVFVVLLGVVWYFRINYRQFFTAPATVSLVGVTVFFSFLVFGMYGR

Signal peptide:

amino acids 1-36

Transmembrane domains:

amino acids 246-267, 275-301

N-glycosylation sites.

amino acids 162-166, 211-215

N-myristoylation sites.

amino acids 48-54, 105-111, 109-115, 129-135, 177-183, 247-253

Cell attachment sequence.

amino acids 97-100

FIGURE 167

GACTCTATTACCTGGCAGAACTGATAGAAGAATACACAGTGGCCACCAGCAGGATCATAAAATACATGATCTGGT TCTCCACCGCTGTACTGATTGGCCTCTACGTCTTTGAGCGCTTCCCCACCAGCATGATTGGAGTGGGCCTATTCA $\tt CCAACCTCGTCTACTTTGGCCTCCTCCAGACCTTCCCCTTCATCATGCTGACCTCGCCTAACTTCATCCTGTCGT$ GTGGACTAGTGGTGGAATCATTACCTAGCATTTCAGTTTTTTGCAGAAGAATATTATCCCTTCTCAGAGGTCC TGGCCTATTTCACTTTCTGCCTGTGGATAATTCCGTTTGCGTTTTTTGTGTCACTTTCGGCCGGGGAGAACGTCC TGCCCTCTACCATGCAGCCAGGAGATGATGTCGTCTCCAATTATTTCACCAAAGGCAAGCGGGGCAAACGCTTAG ${\tt GGATCCTGGTTGTCTTCTCCTTCATCAAAGAGGCCATTCTACCCAGTCGTCAGAAGATATAC\underline{{\tt TGA}}{\tt CCCCCATGCA}}$ GGCAGGATGTGGGGGGCAAGATCAGGAGAGTCAGGCCCCTGGGCCTCTATGCCAGGTGGGGACCAGAAGTCGGGA AGGCACCTACCACCTGCCTGGCTTTCTTCCCCTCAACTCTGGAGCCCCATCCCCACCCTCCTTGGGGGGGCTCAG $\tt CTTGGCTCAGATCTGATGCTTCAAGAGGCTGTAACCTCAGAGGGCACCAAGGAGGGTGGCAGAGCCTGCTTAGCC$ AGGAGGCCGAGGTCCCTCAGTCCTCTCTCCCAAGGTGGGTCAGGAGGTTCTGGCCCCGCTGGGGCAGG GCTTGGCATGTCCAACAGAAATAGTTTTTGCTGTTGAACGGTGATTTCTGTCCAAGTGCAGATTTCCGTTTGAAT AAAGCTTCGCTTCTAGGTGGCACTGTTTGCCTTAATACCCTGACAGTTCATCTTCCTTTCTTCCTGCTAACCTTC TGCTCTGGACTGGACTCACTTTTCTGCTCCAGGGACTCCTTTTCTGGGTTTTGGGTCTTGCCCTTCCCAAGGGACT GTTCTTGTGGCCCTTAATGGGAAGGGGGCAGGGGTGAGGAGCTGAGCCTGCTCAAGGAGTGGGAAGTGGGGCTAT AGGCAGCCTCTCTGATGCACTCTCTTCCATCTCTTTCCCCAAGGCTCCGTGACTGTCAAACTGGGAGTAGGAGAG GGGACAATTTAGGACTGGGCTAGATTTTCAGAAGAACATCTACAATATCCTATTTATAAATCTTCCTCTGGGAAA AGGAGTGGTTTCTGGCTGAATACTATCTTAGGCTCAAGGAGAAACAAAATAAAAATTAGCTTCCAGGCAGCCTGT TTTTAAAGAAATGGGACTAATGGGAGAAGCTGTTTGTCACTCTAAGAGCATCCAAGCCCTGGCCCGTCTGTGCAC CCTTGCACTCCAACTATAGTGCCTTGCAAGTGCTCAACAGTACATATTGGAATGAAGTCCCTATGAGAGCCATTT CTGGCCATGTTCTATACCTCAAAGTGAGGCTGGCAGGTACAGAGATGAACTGTACACATGTGATACATTTAAGCC ACTGGAAAAACCCCTGTGCTTGAAAATATTTCCTCTATATCATGCCTGGAGTTCCATCATAGCCCTTCATTTCCT TGGCTTTAGCATTTACCTTCTTTAAGAATACCAGCTTTCCCCTTTCCCTGAGAGGAAGAGCACATGTTGGTCTC CTCTTAGTGTGAACGAGATTGCCAGGCCCTTTTCTCCTATGCACACCAGGATAGACAAGGCAGGGGATACTGGCA GATGTGGCTTCGCCCCTCCACTCTACTGCCAGTGTTCTCCCAGGGGTTGCTAAATCCAGCAGACCCCTTTCCTG ${\tt TCTTACTAGATCTGGGCAGCATTTGACATGGCTGATCACCCCTTGCTTCTTGGATGGCACTTCCCTGGCACCTCT}$ GTGGCTAGTTGTCCTACCTCCCTGGCTGTTCCTTTCAGGCTTCCGTGCAGGCTTCTCCACTTGCCCATGCACAGT ACAATTCAGGTCCATGGCCCAGATGGTACTTGCTGTCTTCTGCAAACCTGCCCCTTCTGGGTACTTCCCTTGACC CCGAGATCACTCAGGAGCCAGCAGGAAACTTATTCTATTCCTGTTTTCTCTTTCTGCCCACCACCATCCAATCTC ${\tt TCAAAACGGTCAGGTCTACCTTAACATCTCTTGATTTGAGCCACTCCCACTGTCATCAGCTTTCACCTGGATTAT}$ $\tt CGTGACAGCCTCCTACTGCTTCTCTATCATGTGGCCAGAGCTATCTTCCTAAAATGCATTGCATAGTTGATCAAG$ TCACTCTCTGGCCTAAAACCTTCCTTGGCTCCCTGCTCCCTCAGGATAAAGTCTGGACCCCTCAGCATGGCTTG TGAGACTCATGGTGTCCTTGTCCCTGCTCACCTCTCTGGTCTCATCACTTGCCTTCTTGCATTCTGGGTCCCAGC ACTTTCTCTGTCAAATCTCAACTTAGACTTGACTTCCTCCAAGGAGCTTTGGCTATACTCTCTCCCCGACCCC TCCTTGAGGGCAAGGATTGTGTTGGAATTTTTGTATTAACAGTGCCTGGCTTGGTGCCTGGCACCTAGAAAGCAC TCAATAAATGTTTGTTTAATGAA

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FIGURE 168

MWFMYLLSWLSLFIQVAFITLAVAAGLYYLAELIEEYTVATSRIIKYMIWFSTAVLIGLYVFE RFPTSMIGVGLFTNLVYFGLLQTFPFIMLTSPNFILSCGLVVVNHYLAFQFFAEEYYPFSEVL AYFTFCLWIIPFAFFVSLSAGENVLPSTMQPGDDVVSNYFTKGKRGKRLGILVVFSFIKEAIL PSRQKIY

Signal peptide:

amino acids 1-25

Transmembrane domain:

amino acids 126-146

Casein kinase II phosphorylation site.

amino acids 145-148

N-myristoylation sites.

amino acids 73-78, 82-87

Amidation sites.

amino acids 168-171, 171-174

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 91-101

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FIGURE 169

CAAAGCCCTACCCTCACCATTCACCAGGTCCTGTGGGAAGAGCAGCGTGGAGGTGGGCTGAGG TTAGAAGGTGCAGAGCGTGGAAGAAGATTGTGAGCTGAGTATTGGACATCTGTTCTTGAATAG TCCCTGGGCCTGCCATAGGAAAGGAAGTTCTCCAGGGTTACAGTTCTTATCCGCGTGAATACA CATGCTCTGTTACGAAAAATTAATCAGGTGCTGCTGTTCCTTCTGATCGTGACCCTCTGTGT GATTCTGTATAAGAAAGTTCATAAGGGGACTGTGCCCAAGAATGACGCAGATGATGAATCCGA GACTCCTGAAGAACTGGAAGAAGAGATTCCTGTGGTGATTTGTGCTGCAGCAGGGAGGATGGG TGCCACTATGGCTGCCATCAATAGCATCTACAGCAACACTGACGCCAACATCTTGTTCTATGT AGTGGGACTCCGGAATACTCTGACTCGAATACGAAAATGGATTGAACATTCCAAACTGAGAGA AATAAACTTTAAAATCGTGGAATTCAACCCGATGGTCCTCAAAGGGAAGATCAGACCAGACTC ATCGAGGCCTGAATTGCTCCAGCCTCTGAACTTTGTTCGATTTTATCTCCCTCTACTTATCCA CCAACACGAGAAAGTCATCTATTTGGACGATGATGTAATTGTACAAGGTGATATCCAAGAACT GTATGACACCACCTTGGCCCTGGGCCACGCGGCGGCTTTCTCAGATGACTGCGATTTGCCCTC TGCTCAGGACATAAACAGACTCGTGGGACTTCAGAACACATATATGGGCTATCTGGACTACCG GAAGAAGGCCATCAAGGACCTTGGCATCAGCCCCAGCACCTGCTCTTTCAATCCTGGTGTGAT TGTTGCCAACATGACAGAATGGAAGCACCAGCGCATCACCAAGCAATTGGAGAAATGGATGCA AAAGAATGTGGAGGAAAACCTCTATAGCAGCTCCCTGGGAGGAGGGGTGGCCACCTCCCAAT GCTGATTGTGTTTCATGGGAAATATTCCACAATTAACCCCCTGTGGCACATAAGGCACCTGGG CTGGAATCCAGATGCCAGATATTCGGAGCATTTTCTGCAGGAAGCTAAATTACTCCACTGGAA TGGAAGACATAAACCTTGGGACTTCCCTAGTGTTCACAACGACTTATGGGAAAGCTGGTTTGT ATTCCCTGTATAGAAATGTGGAATTGTCCCTTTGTAGCCAACTATAACATTGTTCTTTATGAA TATTACCTTTGATACATATGATCCACAATATAAAAACCAAAAACTACTGTGTGCAAATTATAC CTTGGACCATATAGGCATTGATTAACTTCTTTAAGTACATGTGATAACTATGGAAATCAAGAT TATGTGACTGAAAAACATAAAGGAAGACCCATCTAGATAACAGCAATCAACCTGCTTAATT CTGAATGACAATTATATCCACAAATTTTTAAAACTTCTACATGTATTTTTCACATGAAGATCT CCTTAACAGGTTGCCAACCTTTTCTTTTATAAAACTATTACATTTAAAAATATGGACGTCTGAA AAATAAAATATTCATCATTTTTTAAAA

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FIGURE 170

MALLRKINQVLLFLLIVTLCVILYKKVHKGTVPKNDADDESETPEELEEEIPVVICAAAGRMG
ATMAAINSIYSNTDANILFYVVGLRNTLTRIRKWIEHSKLREINFKIVEFNPMVLKGKIRPDS
SRPELLQPLNFVRFYLPLLIHQHEKVIYLDDDVIVQGDIQELYDTTLALGHAAAFSDDCDLPS
AQDINRLVGLQNTYMGYLDYRKKAIKDLGISPSTCSFNPGVIVANMTEWKHQRITKQLEKWMQ
KNVEENLYSSSLGGGVATSPMLIVFHGKYSTINPLWHIRHLGWNPDARYSEHFLQEAKLLHWN
GRHKPWDFPSVHNDLWESWFVPDPAGIFKLNHHS

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 234-238

Tyrosine kinase phosphorylation site.

amino acids 253-261

N-myristoylation sites.

amino acids 63-69, 86-92, 198-204, 218-224, 229-235, 265-271, 266-272

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FIGURE 171

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FIGURE 172

MEPQLGPEAAALRPGWLALLLWVSALSCSFSLPASSLSSLVPQVRTSYNFGRTFLGLDKCNAC IGTSICKKFFKEEIRSDNWLASHLGLPPDSLLSYPANYSDDSKIWRPVEIFRLVSKYQNEISD RRICASASAPKTCSIERVLRKTERFQKWLQAKRLTPDLVQDCHQGQRELKFLCMLR

Signal peptide:

amino acids 1-28

N-glycosylation site.

amino acids 100-103

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 158-161

N-myristoylation sites.

amino acids 56-61, 65-70

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 18-28

Prenyl group binding site (CAAX box).

amino acids 179-182

Leucine zipper pattern.

amino acids 5-26

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FIGURE 173

ACGCGCACGACTAGCCGCTCCCATACAGCACGCCCGGACTCTGTCGTCGCTTAAGGCCACTCC TATTCTACGGCTGACCCCTGGTGGTCACGTGGATCTGTTCGCCACGCAAGTCTGGGTCCTTCG GCGATTGACCGGGGTCCTTGCTGTTCGGGAGCCTCTCCTAAGCTGCCTGTTCGCGCGAGAGTT TGGAGGGGCGGGTTTGGGGTCGGTGTCTGATTGGGGCTCGCACCGCAGCACGCTGGAGTCCCG CTTAGGTACCAGTTAGCGTCAGGGGAGCTGGGTCAGGCGGTCGCCGGGACACCCCGTGTGTGG CAGGCGGCGAAGCGCTCTGGAGAATCCCGGACAGCCCTGCTCCCTGCAGCCAGGTGTAGTTTC GGGAGCCACTGGGGCCAAAGTGAGAGTCCAGCGGTCTTCCAGCGCTTGGGCCACGGCGGCGC TGCTTCTGGGGGCCCTGCTGGGAACCGCCTGGGCTCGGAGGAGCCAGGATCTCCACTGTGGAG CATGCAGGGCTCTGGTGGATGAACTAGAATGGGAAATTGCCCAGGTGGACCCCAAGAAGACCA CCCGCTCAGAGGCCCACCTCACAGAGCTGCTGGAGGAGATATGTGACCGGATGAAGGAGTATG AATCCAGTGAACTGGACCTACAAGGCATCCGAATCGACTCAGATATTAGCGGCACCCTCAAGT TTGCGTGTGAGAGCATTGTGGAGGATACGAGGATGAACTCATTGAATTCTTTTCCCGAGAGG CTGACAATGTTAAAGACAAACTTTGCAGTAAGCGAACAGATCTTTGTGACCATGCCCTGCACA TATCGCATGATGAGCTA**TGA**ACCACTGGAGCAGCCCACACTGGCTTGATGGATCACCCCCAGG AGGGGAAAATGGTGGCAATGCCTTTTATATATTATGTTTTTACTGAAATTAACTGAAAAAAATA TGAAACCAAAAGT

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FIGURE 174

MKGWGWLALLLGALLGTAWARRSQDLHCGACRALVDELEWEIAQVDPKKTIQMGSFRINPDGS QSVVEVPYARSEAHLTELLEEICDRMKEYGEQIDPSTHRKNYVRVVGRNGESSELDLQGIRID SDISGTLKFACESIVEEYEDELIEFFSREADNVKDKLCSKRTDLCDHALHISHDEL

Signal peptide:

amino acids 1-20

N-myristoylation sites.

amino acids 12-18, 16-22, 29-35

Endoplasmic reticulum targeting sequence.

amino acids 179-184

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FIGURE 175

 $\tt CGCAGCGGGGAGTCCTG{\color{red} \underline{\textbf{ATG}}} GCCCGGCATGGGTTACCGCTGCTGCCCCTGCTGTCGCTCCTG$ GTCGGCGCGTGGCTCAAGCTAGGAAATGGACAGGCTACTAGCATGGTCCAACTGCAGGGTGGG AGATTCCTGATGGGAACAAATTCTCCAGACAGCAGAGATGGTGAAGGGCCTGTGCGGGAGGCG ACAGTGAAACCCTTTGCCATCGACATATTTCCTGTCACCAACAAGATTTCAGGGATTTTGTC GTCTCTGATGAGCTGAGAAACAAAGCCACCCAGCCAATGAAGTCTGTACTCTGGTGGCTTCCA CACCCAGTGTTACACGTGAGCTGGAATGACGCCCGTGCCTACTGTGCTTGGCGGGGAAAACGA CTGCCCACGGAGGAGGTGGGAGTTTGCCGCCCGAGGGGGCTTGAAGGGTCAAGTTTACCCA TGGGGGAACTGGTTCCAGCCAAACCGCACCAACCTGTGGCAGGGAAAGTTCCCCAAGGGAGAC AAAGCTGAGGATGCCTTCCATGGAGTCTCCCCAGTGAATGCTTTCCCCGCCCAGAACAACTAC GGGCTCTATGACCTCCTGGGGAACGTGTGGGAGTGGACAGCATCACCGTACCAGGCTGCTGAG CAGGACATGCGCGTCCTCCGGGGGGCATCCTGGATCGACACAGCTGATGGCTCTGCCAATCAC CGGGCCCGGGTCACCACCAGGATGGGCAACACTCCAGATTCAGCCTCAGACAACCTCGGTTTC CGCTGTGCTGCAGACGCAGGCCGCCAGGGGAGCTGTAAGCAGCCGGGTGGTGACAAGGA GAAAAGCCTTCTAGGGTCACTGTCATTCCCTGGCCATGTTGCAAACAGCGCAATTCCAAGCTC GAGAGCTTCAGCCTCAGGAAAGAACTTCCCCTTCCCTGTCTCCCATCCCTCTGTGGCAGGCGC GACGATGGCTGGGGGCCAGGTGTTTCTGTTAGAGGCCAAGTATTATTGACACAGGATTGCAAA CACACAAACAGTTGGAACAGAGCACTCTGAAAGGCCATTTTTTAAGCATTTTAAAAATCTATTC TCTCCCCCTTTCTCCCTGGATGATTCAGGAAGCTGACATTGTTTCCTCAAGGCAGAATTTTCC GTTTCGTGTCCCTCTGAAGGAAACTAGTTTCCACTGTGTAACAGGCAGACATGTAACTATTTA AAGCACAGTTCAGTCCTAAAAGGGTCTGGGAGAACCAGATGATGTACTAGGTGAAGCATTGCA TTGTGGGAATCACAAAGCAAATAGTACTCCAGAAAGACAAATATCAGAAGCTTCCTATTCTTT TTTTTTTTTTTTTTTTTTTGAGACAGGGTCTTTCTCTGTTGCCCAGGCTAGAGTGCACTG GTGATCACGGCTCACTCTAGCCTTGAATTCCTGGGCCCAAGCAATTCTCCCACCTCAGCCTCC TGAGTAGCTGGGACTACAAGTGTGCACCACCATGCCTGGCTAATTTTTTGAATTTTTGTAGTG ATGGGATCTCGCTCTGTTGCCCAGGGTGGTCTCGAACTCCTGGCCTCAAGCGATCCTCCCACC TCGACCTCCCAAAGTGCTGGGATTACAGGTGTGAGCCACCTCGCCTGGGCCCCCTTCTCCATA TGCCTCCAAAAACATGTCCCTGGAGAGTAGCCTGCTCCCACACTGTCACTGGATGTCATGGGG AAAAAAAAAA

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FIGURE 176

MARHGLPLLPLLSLLVGAWLKLGNGQATSMVQLQGGRFLMGTNSPDSRDGEGPVREATVKPFA
IDIFPVTNKDFRDFVREKKYRTEAEMFGWSFVFEDFVSDELRNKATQPMKSVLWWLPVEKAFW
RQPAGPGSGIRERLEHPVLHVSWNDARAYCAWRGKRLPTEEEWEFAARGGLKGQVYPWGNWFQ
PNRTNLWQGKFPKGDKAEDGFHGVSPVNAFPAQNNYGLYDLLGNVWEWTASPYQAAEQDMRVL
RGASWIDTADGSANHRARVTTRMGNTPDSASDNLGFRCAADAGRPPGEL

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 191-195

N-myristoylation sites.

amino acids 23-29, 25-31, 175-181

Amidation site.

amino acids 159-163

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FIGURE 177

GCCTTCTCGCGCCTGACCATGCACCCCTGCATCTTCCTGCTGGGCCACAGGCGAGCGCTTTAT TTCTGGAGCTGAGGGCTAAAACTTTTTTGACTTTTCTCCTCCAACATCTGAATCATGCCAT GTGCCCAGAGGAGCTGGCTTGCAAACCTTTCCGTGGTGGCTCAGCTCCTTAACTTTGGGGCGC TTTGCTATGGGAGACAGCCTCAGCCAGGCCCGGTTCGCTTCCCGGACAGGAGCAAGAGCATT TTATCAAGGGCCTGCCAGAATACCACGTGGTGGGTCCAGTCCGAGTAGATGCCAGTGGGCATT TTTTGTCATATGGCTTGCACTATCCCATCACGAGCAGCAGGAGAAGAGAGATTTGGATGGCT CAGAGGACTGGGTGTACTACAGAATTTCTCACGAGGAGAAGGACCTGTTTTTTAACTTGACGG TCAATCAAGGATTTCTTTCCAATAGCTACATCATGGAGAAGAGATATGGGAACCTCTCCCATG TTAAGATGATGGCTTCCTCTGCCCCCCTCTGCCATCTCAGTGGCACGGTTCTACAGCAGGGCA ACATCGTTTACAGGAGGCAGAAAGTTCCAGAAACCAAGGAGCCAACCTGTGGATTAAAGGGTA $\tt TTGTGACTCACATGTCCTCCTGGGTTGAAGAATCTGTTTTTGTTCTTTTTGG\underline{\textbf{TAG}} \tt TTTTATTAAA$ TGACATTCAAATCTCTTCTGTATTCTCTTGCCAGAAAGTGTACATTCTTTTTGCTTGTATAAA CCCTTTCACTTGTC

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FIGURE 178

MPCAQRSWLANLSVVAQLLNFGALCYGRQPQPGPVRFPDRRQEHFIKGLPEYHVVGPVRVDAS GHFLSYGLHYPITSSRRKRDLDGSEDWVYYRISHEEKDLFFNLTVNQGFLSNSYIMEKRYGNL SHVKMMASSAPLCHLSGTVLQQGTRVGTAALSACHGLTGFFQLPHGDFFIEPVKKHPLVEGGY HPHIVYRRQKVPETKEPTCGLKGIVTHMSSWVEESVLFFW

Signal peptide:

amino acids 1-27

N-glycosylation sites.

amino acids 11-15, 105-109, 125-129

N-myristoylation site.

amino acids 149-155

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FIGURE 179

CAGATTTAAAAAGAAAACCTTTACTGAATCAGCTGAGTGTTAATAATACGAATTTCCTTTTCT TGCCAATTCTGATCTGAACAGAAAATCCAAGAACAGGGAT**ATG**TGTGGATTACAGTTTTCTCT GCCTTGCCTACGACTGTTTCTGGTTGTTACCTGTTATCTTTTATTATTACTCCACAAAGAAAT ACTTGGATGTTCGTCTGTTTGTCAGCTCTGCACTGGGAGACAAATTAACTGCCGTAACTTAGG CCTTTCGAGTATTCCTAAGAATTTTCCTGAAAGTACAGTTTTTCTGTATCTGACTGGGAATAA TATATCTTATATAAATGAAAGTGAATTAACAGGACTTCATTCTCTTGTAGCATTGTATTTGGA TAATTCTAACATTCTGTATGTATATCCAAAAGCCTTTGTTCAATTGAGGCATCTATATTTTCT ATTTCTAAATAATTTCATCAAACGCTTAGATCCTGGAATATTTAAGGGACTTTTAAATCT TCGTAATTTATATTTACAGTATAATCAGGTATCTTTTGTTCCGAGAGGAGTATTTAATGATCT AGTTTCAGTTCAGTACTTAAATCTACAAAGGAATCGCCTCACTGTCCTTGGGAGTGGTACCTT TGTTGGTATGGTTGCTCTTCGGATACTTGATTTATCAAACAATAACATTTTGAGGATATCAGA ATCAGGCTTTCAACATCTTGAAAACCTTGCTTGTTTGTATTTAGGAAGTAATAATTTAACAAA TATTGAAGCAATACAGCCCTTTGCATTTAAAGGACTTGCCAATCTGGAATACCTCCTCCTGAA AAATTCAAGAATTAGGAATGTTACTAGGGATGGGTTTAGTGGAATTAATAATCTTAAACATTT GATCTTAAGTCATAATGATTTAGAGAATTTAAATTCTGACACATTCAGTTTGTTAAAGAATTT AATTTACCTTAAGTTAGATAGAAACAGAATAATTAGCATTGATAATGATACATTTGAAAAATAT GGGAGCATCTTTGAAGATCCTTAATCTGTCATTTAATAATCTTACAGCCTTGCATCCAAGGGT CCTTAAGCCGTTGTCTTCATTGATTCATCTTCAGGCAAATTCTAATCCTTGGGAATGTAACTG CAAACTTTTGGGCCTTCGAGACTGGCTAGCATCTTCAGCCATTACTCTAAACATCTATTGTCA GAATCCCCCATCCATGCGTGGCAGAGCATTACGTTATATTAACATTACAAATTGTGTTACATC TTCAATAAATGTATCCAGAGCTTGGGCTGTTGTAAAATCTCCTCATATTCATCACAAGACTAC TGCGCTAATGATGGCCTGGCATAAAGTAACCACAAATGGCAGTCCTCTGGAAAATACTGAGAC TGAGAACATTACTTTCTGGGAACGAATTCCTACTTCACCTGCTGGTAGATTTTTTCAAGAGAA TGCCTTTGGTAATCCATTAGAGACTACAGCAGTGTTACCTGTGCAAATACAACTTACTACTTC TGTTACCTTGAACTTGGAAAAAAACAGTGCTCTACCGAATGATGCTGCTTCAATGTCAGGGAA AACATCTCTAATTTGTACACAAGAAGTTGAGAAGTTGAATGAGGCTTTTGACATTTTGCTAGC TTTTTTCATCTTAGCTTGTGTTTTAATCATTTTTTTTGATCTACAAAGTTGTTCAGTTTAAACA AAAACTAAAGGCATCAGAAAACTCAAGGGAAAATAGACTTGAATACTACAGCTTTTATCAGTC AGCAAGGTATAATGTAACTGCCTCAATTTGTAACACTTCCCCAAATTCTCTAGAAAGTCCTGG CTTGGAGCAGATTCGACTTCATAAACAAATTGTTCCTGAAAATGAGGCACAGGTCATTCTTTT TGAACATTCTGCTTTA**TAA**CTCAACTAAATATTGTCTATAAGAAACTTCAGTGCCATGGACAT GATTTAAACTGAAACCTCCTTATATAATTATATACTTTAGTTGGAAATATAATGAATTATATG

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FIGURE 180

MCGLQFSLPCLRLFLVVTCYLLLLLHKEILGCSSVCQLCTGRQINCRNLGLSSIPKNFPESTV
FLYLTGNNISYINESELTGLHSLVALYLDNSNILYVYPKAFVQLRHLYFLFLNNNFIKRLDPG
IFKGLLNLRNLYLQYNQVSFVPRGVFNDLVSVQYLNLQRNRLTVLGSGTFVGMVALRILDLSN
NNILRISESGFQHLENLACLYLGSNNLTKVPSNAFEVLKSLRRLSLSHNPIEAIQPFAFKGLA
NLEYLLKNSRIRNVTRDGFSGINNLKHLILSHNDLENLNSDTFSLLKNLIYLKLDRNRIISI
DNDTFENMGASLKILNLSFNNLTALHPRVLKPLSSLIHLQANSNPWECNCKLLGLRDWLASSA
ITLNIYCQNPPSMRGRALRYINITNCVTSSINVSRAWAVVKSPHIHHKTTALMMAWHKVTTNG
SPLENTETENITFWERIPTSPAGRFFQENAFGNPLETTAVLPVQIQLTTSVTLNLEKNSALPN
DAASMSGKTSLICTQEVEKLNEAFDILLAFFILACVLIIFLIYKVVQFKQKLKASENSRENRL
EYYSFYQSARYNVTASICNTSPNSLESPGLEQIRLHKQIVPENEAQVILFEHSAL

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 530-547

N-glycosylation sites.

amino acids 71-75, 76-80, 215-219, 266-270, 317-321, 331-335, 336-340, 400-404, 410-414, 451-455, 579-583

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 231-235

N-myristoylation sites.

amino acids 3-9, 69-75, 126-132, 174-180

ATP/GTP-binding site motif A (P-loop).

amino acids 506-514

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FIGURE 181

GGCCTGGCGCGCGCTCCGGTAAGGCGTGTGTGCGGCAGGGCGGGGACAGAACCGTCCTCTCG GGCTCTGGGCGTGTCCGAGACCGCGCTCCCCGCCGAAATCAAGCTCCGAGTCATCCGTGTGGG GCATTCGTCCCCCTGGCACAGTTGGCCTCTTTCCAGAAGCCCGTTTTGTTTTGTTTTACGTCT AAATTCGCGTCGGTTCTTATTTCTCTCCCTGGCAAGGTCTGAAGACGGGTAGGAGAATAACCT $\tt GTGTCAGCGTGTT{\color{red} \underline{ATG}} ATGCCGTCCCGTACCAACCTGGCTACTGGAATCCCCAGTAGTAAAGT$ GAAATATTCAAGGCTCTCCAGCACAGACGATGGCTACATTGACCTTCAGTTTAAGAAAACCCC TCCTAAGATCCCTTATAAGGCCATCGCACTTGCCACTGTGCTGTTTTTGATTGGCGCCCTTTCT CATTATTATAGGCTCCCTCCTGCTGTCAGGCTACATCAGCAAAGGGGGGGCAGACCGGGCCGT TCCAGTGCTGATCATTGGCATTCTGGTGTTCCTACCCGGATTTTACCACCTGCGCATCGCTTA $\tt CTATGCATCCAAAGGCTACCGTGGTTACTCCTATGATGACATTCCAGACTTTGATGAC{\color{red}{\bf TAG}CA}$ CCCACCCCATAGCTGAGGAGGAGTCACAGTGGAACTGTCCCAGCTTTAAGATATCTAGCAGAA ACTATAGCTGAGGACTAAGGAATTCTGCAGCTTGCAGATGTTTAAGAAAATAATGGCCAGATT TTTTGGGTCCTTCCCAAAGATGTTAAGTGAACCTACAGTTAGCTAATTAGGACAAGCTCTATT TTTCATCCCTGGGCCCTGACAAGTTTTTCCACAGGAATATGTATCATGGAAGAATAGAGGTTA TTCTGTAATGGAAAAGTGTTGCCTGCCACCACCTCTGTAGAGCTGAGCATTTCTTTTAAATA GTCTTCATTGCCAATTTGTTCTTGTAGCAAATGGAACAATGTGGTATGGCTAATTTCTTATTA TTAAGTAGTTTATTTTAAAAATATCTGAGTATATTATCCTGTACACTTATCCCTACCTTCATG TGCTTTCTTACTGACAGCAACCAGGAATTTTTTTTATCCTGCAGAGCAAGTTTTCAAAATGTAA ATACTTCCTCTGTTTAACAGTCCTTGGACCATTCTGATCCAGTTCACCAGTAGGTTGGACAGC ATATAATTTGCATCATTTTGTCCCTTGTAAATCAAGATGTTCTGCAGATTATTCCTTTAACGG CCGGACTTTTGGCTGTTTCCTAATGAAACATGTAGTGGTTATTATTTAGAGTTTATAGCCGTA TTGCTAGCACCTTGTAGTATGTCATCATTCTGCTCATGATTCCAAGGATCAGCCTGGATGCCT AGAGGACTAGATCACCTTAGTTTGATTCTATTTTTTAGCTTGCAAAAAGTGACTTATATTCCA

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FIGURE 182

MMPSRTNLATGIPSSKVKYSRLSSTDDGYIDLQFKKTPPKIPYKAIALATVLFLIGAFLIIIG SLLLSGYISKGGADRAVPVLIIGILVFLPGFYHLRIAYYASKGYRGYSYDDIPDFDD

Transmembrane domains:

amino acids 45-66, 79-95

N-myristoylation sites.

amino acids 11-17, 75-81

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FIGURE 183

CTAAAAAATACAAAAATTAGCTGGGCGTGGTGTCATGTACCTGTAATCCCAGCTACTCAAGAGGCTGAGGCAGGA GAATCGCTTGAACCCAGGAGGCAGAGGTTGCAGTGAGCCAAGATTAAGTCACTGCACTCCAGCCTGGGTGACAGA GCAAGACTCTGTATCAAAATAAATAAATAAAGTACAACTCTGGATGGGCATGGTGGCTTATGTCTGTAATCCCAG CACTTTGGGAACTTGAGGCGGGTAGATTGCTTGAGTCCGGGAGTTTGAGACCAGTCTGGGTAATATGGTAACCCT AAAATTTAAAAAATAAAGTCCAACTCAGCGGTTTTCAGCATATTTACAGAGTTGTACAATCTTCACCACTATCTA CCTCTGGCAACCACTAATCTCTTTTTTGTCTCTATAGATTTGCCTATTTTGGACAGTTCATATACAAGGAATCAT ACCACATGTAGCCTTTTGTGTCCGGCTTCTTTGATTAATAGAATGTTTTCAAGGCTCATCTATGCTGTAGCCTGT ATCAGCACTTCATTCCTTTCTATGGCTGAATAATAGTCCACTGTAGGGATGTCCATGTTTTTCCACTAGCTGAT GGACATTTGGGTTGTTTCCACCTTCTGGCTATTATAAATATTGCTGCTATAAATATTCACTTACAAGTTTTTGTG TGGACATATGTTTTTATTTCTTCTGGTATATCCTTCGGAGTGGAACTGCTGGATCAGGTGGTAACTCTAGGTCTA ACCTGGCAGTTAAACAGAATCCTATGCATGCTGTAGTCCATGAGTTGAAATAAACACTTGACCCATAGTAAGTGC CAGATCATCTTCATTTCACAGCAACCAGTAATTTCACAGATGAGGAAATGAAGGCTCCCAGAGGTGAACTGGCTT TTCCCATTTGAGCAGTTCCAAGTCAGACAGTTAAAAAGTGGCAGGACCTGGAAGAGAAGCTAGTTCTTTCACCCT GGCATTCAGGGCTGCCTCCTGGGCTACGGGGCTGGCATTTAGAATAGAGCTAAGGTCTGCTGCCAAGGCAGGTGC CCCAGTCTGCCTCTGTGTCCTTATTCCACTTTCTCTGCAGCCCTCCAGGGGACCCCTCTCTCAGCCACCCTC TCTCTGGTG<u>ATG</u>TCACAGTGCTGCCGGAAGATCAAAGATACGGTGCAGAAACTGGCTTCGGACCATAAGGACATT CACAGCAGTGTATCCCGAGTGGGCAAAGCCATTGACAGGAACTTCGACTCTGAGATCTGTGGTGTTGTCAGAT GCGGTGTGGGACGCGGGAACAGCAGCAGCAGATCCTGCAGATGGCCATCGTGGAACACCTGTATCAGCAGGGC ATGCTCAGCGTGGCCGAGGAGCTGTGCCAGGAATCAACGCTGAATGTGGACTTGGATTTCAAGCAGCCTTTCCTA GAGTTGAATCGAATCCTGGAAGCCCTGCACGAACAAGACCTGGGTCCTGCGTTGGAATGGGCCGTCTCCCACAGG CAGCGCCTGCTGGAACTCAACAGCTCCCTGGAGTTCAAGCTGCACCGACTGCACTTCATCCGCCTCTTGGCAGGA GGCCCGCGAAGCAGCTGGAGGCCCTCAGCTATGCTCGGCACTTCCAGCCCTTTGCTCGGCTGCACCAGCGGGAG ATCCAGGTGATGATGGGCAGCCTGGTGTACCTGCGGCTGGGCTTGGAGAAGTCACCCTACTGCCACCTGCTGGAC CCCCTTAGCGTCAGCTTTGCCTCTGGCTGTGTGGCGCTGCCTGTGTTGATGAACATCAAGGCTGTGATTGAGCAG CGGCAGTGCACTGGGGTCTGGAATCACAAGGACGAGTTACCGATTGAGATTGAACTAGGCATGAAGTGCTGGTAC GCTCATCTGTGGCCATGTTATCTCCCGAGATGCACTCAATAAGCTCATTAATGGAGGAAACACTCCGTGTTCGCT TGCCCCATCCTCCGCCAGCAGACGTCAGATTCCAACCCTCCCATCAAGCTGAAGTGTCCCTACTGTCCCATGGAG ${\tt CAGAACCCGGCAGATGGGAAACGCATCATATTC} \underline{{\tt TGA}}{\tt TTCCTACCTGGAAGGAATTTTGTTGAAAGGGGTTTTCAC}$ GAGTTCCACTGAGGGGAGCACTGGAGCAGCCCTTTGGCAGAGGCTGAGGAGGAGATGGACCAGCCCACGCCTGG CACCTGGCTCCATGGCATAAGGAAAGGGAGATGCTGGCCTCTGTGCTCCTGCTGTTTTCCTGTTTTGC GTTTGACTTAGTAGCAACCGACAGAGTGGCAAGGGATTTGGTCTTCAGCAGTAGACATCCTTCCACCCCTGCCCT CACCTCTTCCTCCCACTACAGCCTCAACAGTATGTACCATCTCCCACTGTAAATAGTCCCAGTTAGAACGGAATG ${\tt CCGTTGTTTTATAACTTTGAACAAATGTATTTACTGCCCTTCTCAAAA}$

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FIGURE 184

QCCRKIKDTVQKLASDHKDIHSSVSRVGKAIDRNFDSEICGVVSDAVWDAREQQQQILQMAIV EHLYQQGMLSVAEELCQESTLNVDLDFKQPFLELNRILEALHEQDLGPALEWAVSHRQRLLEL NSSLEFKLHRLHFIRLLAGGPAKQLEALSYARHFQPFARLHQREIQVMMGSLVYLRLGLEKSP YCHLLDSSHWAEICETFTRDACSLLGLSVESPLSVSFASGCVALPVLMNIKAVIEQRQCTGVW NHKDELPIEIELGMKCWYHSVFACPILRQQTSDSNPPIKLICGHVISRDALNKLINGGKLKCP YCPMEQNPADGKRIIF

Transmembrane domain:

amino acids 222-241

N-glycosylation site.

amino acids 129-133

Tyrosine kinase phosphorylation site.

amino acids 151-159, 184-193

Amidation site.

amino acids 327-331

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 222-233

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FIGURE 185

GAGCGACGCTGTCTCTAGTCGCTGATCCCAA**ATG**CACCGGCTCATCTTTGTCTACACTCTAAT TTTGCGCAACGCCAACCTCAGGCGAGATGACTTGTACCGAAGAGATGAGACCATCCAGGTGAA AGGAAACGGCTACGTGCAGAGTCCTAGATTCCCGAACAGCTACCCCAGGAACCTGCTCCTGAC ATGGCGGCTTCACTCTCAGGAGAATACACGGATACAGCTAGTGTTTGACAATCAGTTTGGATT AGAGGAAGCAGAAAATGATATCTGTAGGTATGATTTTTGTGGAAGTTGAAGATATATCCGAAAC CAGTACCATTATTAGAGGACGATGGTGTGGACACAAGGAAGTTCCTCCAAGGATAAAATCAAG AACGAACCAAATTAAAATCACATTCAAGTCCGATGACTACTTTGTGGCTAAACCTGGATTCAA GATTTATTATTCTTTGCTGGAAGATTTCCAACCCGCAGCAGCTTCAGAGACCAACTGGGAATC TGTCACAAGCTCTATTTCAGGGGTATCCTATAACTCTCCATCAGTAACGGATCCCACTCTGAT TGCGGATGCTCTGGACAAAAAATTGCAGAATTTGATACAGTGGAAGATCTGCTCAAGTACTT CAATCCAGAGTCATGGCAAGAAGATCTTGAGAATATGTATCTGGACACCCCTCGGTATCGAGG CAGGTCATACCATGACCGGAAGTCAAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCG TTACAGTTGCACTCCCAGGAATTACTCGGTCAATATAAGAGAAGAGCTGAAGTTGGCCAATGT GGTCTTCTTTCCACGTTGCCTCCTCGTGCAGCGCTGTGGAGGAAATTGTGGCTGTGGAACTGT CAACTGGAGGTCCTGCACATGCAATTCAGGGAAAACCGTGAAAAAGTATCATGAGGTATTACA GTTTGAGCCTGGCCACATCAAGAGGGGGGTAGAGCTAAGACCATGGCTCTAGTTGACATCCA ${\tt GTTGGATCACCATGAACGATGCGATTGTATCTGCAGCTCAAGACCACCTCGA} {\color{red}{\textbf{TAA}}} {\tt GAGAATGT}$ GCACATCCTTACATTAAGCCTGAGAGAA

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FIGURE 186

MHRLIFVYTLICANFCSCRDTSATPQSASIKALRNANLRRDDLYRRDETIQVKGNGYVQSPRF
PNSYPRNLLLTWRLHSQENTRIQLVFDNQFGLEEAENDICRYDFVEVEDISETSTIIRGRWCG
HKEVPPRIKSRTNQIKITFKSDDYFVAKPGFKIYYSLLEDFQPAAASETNWESVTSSISGVSY
NSPSVTDPTLIADALDKKIAEFDTVEDLLKYFNPESWQEDLENMYLDTPRYRGRSYHDRKSKV
DLDRLNDDAKRYSCTPRNYSVNIREELKLANVVFFPRCLLVQRCGGNCGCGTVNWRSCTCNSG
KTVKKYHEVLQFEPGHIKRRGRAKTMALVDIQLDHHERCDCICSSRPPR

Signal peptide:

amino acids 1-18

N-glycosylation site.

amino acids 270-274

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 262-266

Tyrosine kinase phosphorylation site.

amino acids 256-265

N-myristoylation sites.

amino acids 94-100, 186-192, 297-303, 298-304

TonB-dependent receptor proteins signature 1.

amino acids 1-56

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FIGURE 187

 $\texttt{C}\underline{\textbf{ATG}}\texttt{CCGCTGCTGCTGTTGCTCCTGGCGGCGCCTTGGGGGACGGCAGTTCCCTG}$ TGTCTCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGAATGT CATATATGGGCAAAAGAATGGCTGAATAAATCAGAATGCAGAAATATCAATAGAACCTACTG TGATCTTTCTGCTGAAACTTCTGACTACGAACACCAGTATTATGCCAAAGTTAAGGCCATTTG GGGAACAAGTGTTCCAAATGGGCTGAAAGTGGACGGTTCTATCCTTTTTTAGAAACACAAAT TGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGTCCTGACAGCTCC AGAGAAGTGGAAGAGAATCCAGAAGACCTTCCTGTTTCCATGCAACAAATATACTCCAATCT GAAGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCCCAGTGTGTGACCAA CCACACGCTGGTGCTCACCTGGCTGGAGCCGAACACTCTTTACTGCGTACACGTGGAGTCCTT CGTCCCAGGGCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTGCCAGGACTTTGAAAGA TCAATCATCAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTGCCCATATCTATTACCGT GTTTCTTTTTCTGTGATGGGCTATTCCATCTACCGATATATCCACGTTGGCAAAGAGAAACA CCCAGCAAATTTGATTTTGATTTATGGAAATGAATTTGACAAAAGATTCTTTGTGCCTGCTGA AAAAATCGTGATTAACTTTATCACCCTCAATATCTCGGATGATTCTAAAATTTCTCATCAGGA TATGAGTTTACTGGGAAAAAGCAGTGATGTATCCAGCCTTAATGATCCTCAGCCCAGCGGGAA CCTGAGGCCCCCTCAGGAGGAAGAGGAGGTGAAACATTTAGGGTATGCTTCGCATTTGATGGA AATTTTTTGTGACTCTGAAGAAAACACGGAAGGTACTTCTCTCACCCAGCAAGAGTCCCTCAG CAGAACAATACCCCCGGATAAAACAGTCATTGAATATGAATATGATGTCAGAACCACTGACAT TTGTGCGGGGCCTGAAGAGCAGGAGCTCAGTTTGCAGGAGGAGGTGTCCACACAAGGAACATT ATTGGAGTCGCAGCGTTGGCAGTCTTGGGCCCGCAAACGTTACAGTACTCATACACCCC TCAGCTCCAAGACTTAGACCCCCTGGCGCAGGAGCACACAGACTCGGAGGAGGGGCCGGAGGA AGAGCCATCGACGACCCTGGTCGACTGGGATCCCCAAACTGGCAGGCTGTGTATTCCTTCGCT GTCCAGCTTCGACCAGGATTCAGAGGGCTGCGAGCCTTCTGAGGGGGATGGGCTCGGAGAGGA GGGTCTTCTATCTAGACTCTATGAGGAGCCGGCTCCAGACAGGCCACCAGGAGAAAATGAAAAC CTATCTCATGCAATTCATGGAGGAATGGGGGTTATATGTGCAGATGGAAAAC<u>TGA</u>TGCCAACA CTTCCTTTTGCCTTTTGTTTCCTGTGCAAACAAGTGAGTCACCCCTTTGATCCCAGCCATAAA GTACCTGGGATGAAAGAAGTTTTTTCCAGTTTGTCAGTGTCTGTGAGAA

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FIGURE 188

MPLPPLLLLLAAPWGRAVPCVSGGLPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQYF
IYGQKKWLNKSECRNINRTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWAESGRFYPFLETQI
GPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQQIYSNLKYNVSVLNTKSNRTWSQCVTN
HTLVLTWLEPNTLYCVHVESFVPGPPRRAQPSEKQCARTLKDQSSEFKAKIIFWYVLPISITV
FLFSVMGYSIYRYIHVGKEKHPANLILIYGNEFDKRFFVPAEKIVINFITLNISDDSKISHQD
MSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKHLGYASHLMEIFCDSEENTEGTSLTQQESLS
RTIPPDKTVIEYEYDVRTTDICAGPEEQELSLQEEVSTQGTLLESQAALAVLGPQTLQYSYTP
QLQDLDPLAQEHTDSEEGPEEEPSTTLVDWDPQTGRLCIPSLSSFDQDSEGCEPSEGDGLGEE
GLLSRLYEEPAPDRPPGENETYLMQFMEEWGLYVQMEN

Signal sequence:

amino acids 1-18

Transmembrane domain:

amino acids 240-260

N-glycosylation sites.

amino acids 31-34, 72-75, 80-83, 171-174, 180-183, 189-192, 304-307, 523-526

Tyrosine kinase phosphorylation site.

amino acids 385-392, 518-526

N-myristoylation sites.

amino acids 53-58, 106-111, 368-373, 492-497

Tissue factor

amino acids 1-278

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FIGURE 189

CAGCGGGGCAGCCAGATCGCCTTCCGCCTCCAGGTGCGCACTGCAGGCTACGTGGGCTTCGGC TTCTCGCCCACCGGGGCCATGGCGTCCGCCGACATCGTCGTGGGCGGGGTGGCCCACGGGCGG CCCTACCTCCAGGATTATTTTACAAATGCAAATAGAGAGTTGAAAAAAGATGCTCAGCAAGAT TACCATCTAGAATATGCCATGGAAAATAGCACACACACAATAATTGAATTTACCAGAGAGCTG CATACATGTGACATAAATGACAAGAGTATAACGGATAGCACTGTGAGAGTGATCTGGGCCTAC CACCATGAAGATGCAGGAGAAGCTGGTCCCAAGTACCATGACTCCAATAGGGGCACCAAGAGT TTGCGGTTATTGAATCCTGAGAAAACTAGTGTGCTATCTACAGCCTTACCATACTTTGATCTG GTAAATCAGGACGTCCCCATCCCAAACAAAGATACAACATATTGGTGCCAAATGTTTAAGATT CCTGTGTTCCAAGAAAAGCATCATGTAATAAAGGTTGAGCCAGTGATACAGAGAGGCCATGAG AGTCTGGTGCACCACATCCTGCTCTATCAGTGCAGCAACAACTTTAACGACAGCGTTCTGGAG TCCGGCCACGAGTGCTATCACCCCAACATGCCCGATGCATTCCTCACCTGTGAAACTGTGATT TTTGCCTGGGCTATTGGTGGAGAGGGCTTTTCTTATCCACCTCATGTTGGATTATCCCTTGGC ACTCCATTAGATCCGCATTATGTGCTCCTAGAAGTCCATTATGATAATCCCACTTATGAGGAA GGCTTAATAGATAATTCTGGACTGAGGTTATTTTACACAATGGATATAAGGAAATATGATGCT GGGGTGATTGAGGCTGGCCTCTGGGTGAGCCTCTTCCATACCATCCCTCCAGGGATGCCTGAG TTCCAGTCTGAGGGTCACTGCACTTTGGAGTGCCTGGAAGAGGCTCTGGAAGCCGAAAAGCCA CGTCATTTTCGAAAAGGGAAGGAAATGAAATTACTTGCCTATGATGATGATTTTTGACTTCAAT TTCCAGGAGTTTCAGTATCTAAAGGAAGAACAACCATCTTACCAGGAGATAACCTAATTACT GAGTGTCGCTACAACACGAAAGATAGAGCTGAGATGACTTGGGGAGGACTAAGCACCAGGAGT GAAATGTGTCTCTCATACCTTCTTTATTACCCAAGAATTAATCTTACTCGATGTGCAAGTATT CCAGACATTATGGAACAACTTCAGTTCATTGGGGTTAAGGAGATCTACAGACCAGTCACGACC AAGTTTAAATGGACTAAAAAGGAAGGTCTCTCCTTCAACAAGCTGGTCCTCAGCCTGCCAGTG AATGTGAGATGTTCCAAGACAGACAATGCTGAGTGGTCGATTCAAGGAATGACAGCATTACCT CCAGATATAGAAAGACCCTATAAAGCAGAACCTTTGGTGTGTGGCACGTCTTCTTCCTCTTCC CTGCACAGAGATTTCTCCATCAACTTGCTTGTTTGCCTTCTGCTACTCAGCTGCACGCTGAGC ACCAAGAGCTTG<u>TGA</u>TCAAAATTCTGTTGGACTTGACAATGTTTTCTATGATCTGAACCTGTC ATTTGAAGTACAGGTTAAAGACTGTGTCCACTTTGGGCATGAAGAGTGTGGAGACTTTTCTTC CTCTTTCTTAGAAATACCTGATGTTATATATATACATGGTCAATAAAATAAAACTGGCCTGACTT AAAAAAA

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FIGURE 190

MCCWPLLLLWGLLPGTAAGGSGRTYPHRTLLDSEGKYWLGWSQRGSQIAFRLQVRTAGYVGFG
FSPTGAMASADIVVGGVAHGRPYLQDYFTNANRELKKDAQQDYHLEYAMENSTHTIIEFTREL
HTCDINDKSITDSTVRVIWAYHHEDAGEAGPKYHDSNRGTKSLRLLNPEKTSVLSTALPYFDL
VNQDVPIPNKDTTYWCQMFKIPVFQEKHHVIKVEPVIQRGHESLVHHILLYQCSNNFNDSVLE
SGHECYHPNMPDAFLTCETVIFAWAIGGEGFSYPPHVGLSLGTPLDPHYVLLEVHYDNPTYEE
GLIDNSGLRLFYTMDIRKYDAGVIEAGLWVSLFHTIPPGMPEFQSEGHCTLECLEEALEAEKP
SGIHVFAVLLHAHLAGRGIRLRHFRKGKEMKLLAYDDDFDFNFQEFQYLKEEQTILPGDNLIT
ECRYNTKDRAEMTWGGLSTRSEMCLSYLLYYPRINLTRCASIPDIMEQLQFIGVKEIYRPVTT
WPFIIKSPKQYKNLSFMDAMNKFKWTKKEGLSFNKLVLSLPVNVRCSKTDNAEWSIQGMTALP
PDIERPYKAEPLVCGTSSSSSLHRDFSINLLVCLLLLSCTLSTKSL

Signal peptide:

amino acids 1-18

Transmembrane domains:

amino acids 56-73, 378-393, 583-602

N-glycosylation sites.

amino acids 114-118, 247-251, 476-480, 517-521

N-myristoylation sites.

amino acids 11-17, 15-21, 20-26, 45-51, 68-74, 79-85, 290-296, 316-322, 337-343, 342-348, 456-462, 534-540, 582-588

Copper type II, ascorbate-dependent monooxygenases proteins.

amino acids 271-321, 422-474

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FIGURE 191

GCTTCAGCTGAAGAAAGAGAGGGA**ATG**AAGCGCCTTCTGCTTCTGTTTTTTGTTCTTTATAACAT TTTCTTCTGCATTTCCCTTAGTCCGGATGACGGAAAATGAAGAAAATATGCAACTGGCTCAGG CATATCTCAACCAGTTCTACTCTTGAAATAGAAGGGAATCATCTTGTTCAAAGCAAGAATA GGAGTCTCATAGATGACAAAATTCGGGAAATGCAAGCATTTTTTGGATTGACAGTGACTGGAA AACTGGACTCAAACACCCTTGAGATCATGAAGACACCCAGGTGTGGGGTGCCTGATGTGGGCC AGTATGGCTACACCCTCCCTGGGTGGAGAAAATACAACCTCACCTACAGAATAATAAACTATA CTCCGGATATGGCACGAGCTGCTGTGGATGAGGCTATCCAAGAAGGTTTAGAAGTGTGGAGCA AAGTCACTCCACTAAAATTCACCAAGATTTCAAAGGGGATTGCAGACATCATGATTGCCTTTA GGACTCGAGTCCATGGTCGGTGTCCTCGCTATTTTGATGGTCCCTTGGGAGTGCTTGGCCATG CCTTTCCTCCTGGTCCGGGTCTGGGTGGTGACACTCATTTTGATGAGGATGAAAACTGGACCA AGGATGGAGCAGGATTCAACTTGTTTCTTGTGGCTGCTCATGAATTTGGTCATGCACTGGGGC TCTCTCACTCCAATGATCAAACAGCCTTGATGTTCCCAAATTATGTCTCCCTGGATCCCAGAA AATACCCACTTTCTCAGGATGATATCAATGGAATCCAGTCCATCTATGGAGGTCTGCCTAAGG TACCTGCTAAGCCAAAGGAACCCACTATACCCCATGCCTGTGACCCTGACTTGACTTTTGACG ATGATATCACGGATGTTGAGTTTGAATTAATTGCTTCATTCTGGCCATCTCTGCCAGCTGATC TGCAAGCTGCATACGAGAACCCCAGAGATAAGATTCTGGTTTTTAAAGATGAAAACTTCTGGA GACGTGTGAAGAAAATAGATGCAGCCGTCTGTGATAAGACCACAAGAAAAACCTACTTCTTTG TGGGCATTTGGTGCTGGAGGTTTGATGAAATGACCCAAACCATGGACAAAGGATTCCCGCAGA GAGTGGTAAAACACTTTCCTGGAATCAGTATCCGTGTTGATGCTGCTTTCCAGTACAAAGGAT TCTTCTTTTCAGCCGTGGATCAAAGCAATTTGAATACAACATTAAGACAAAGAATATTACCC GAATCATGAGAACTAATACTTGGTTTCAATGCAAAGAACCAAAGAACTCCTCATTTGGTTTTG ATATCAACAAGGAAAAAGCACATTCAGGAGGCATAAAGATATTGTATCATAAGAGTTTAAGCT TGTTTATTTTTGGTATTGTTCATTTGCTGAAAAACACTTCTATTTATCAA**TAA**ATTCATAGAC CTAAAATAAACCTCAACAGGTCTTTTAATATAAATTCTGCTTCAAAATAGAATAAAACCATTC TTTAACAAC

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FIGURE 192

MKRLLLLFLFFITFSSAFPLVRMTENEENMQLAQAYLNQFYSLEIEGNHLVQSKNRSLIDDKI REMQAFFGLTVTGKLDSNTLEIMKTPRCGVPDVGQYGYTLPGWRKYNLTYRIINYTPDMARAA VDEAIQEGLEVWSKVTPLKFTKISKGIADIMIAFRTRVHGRCPRYFDGPLGVLGHAFPPGPGL GGDTHFDEDENWTKDGAGFNLFLVAAHEFGHALGLSHSNDQTALMFPNYVSLDPRKYPLSQDD INGIQSIYGGLPKVPAKPKEPTIPHACDPDLTFDAITTFRREVMFFKGRHLWRIYYDITDVEF ELIASFWPSLPADLQAAYENPRDKILVFKDENFWMIRGYAVLPDYPKSIHTLGFPGRVKKIDA AVCDKTTRKTYFFVGIWCWRFDEMTQTMDKGFPQRVVKHFPGISIRVDAAFQYKGFFFFSRGS KQFEYNIKTKNITRIMRTNTWFQCKEPKNSSFGFDINKEKAHSGGIKILYHKSLSLFIFGIVH LLKNTSIYQ

Signal peptide:

amino acids 1-17

N-glycosylation sites.

amino acids 55-59, 110-114, 200-204, 452-456, 470-474, 508-512

N-myristoylation site.

amino acids 71-77, 205-211, 223-229

Hemopexin domain signature.

amino acids 171-202, 207-238, 318-334

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 213-223

Matrixins cysteine switch.

amino acids 89-97, 207-238

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FIGURE 193

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FIGURE 194

MVLGNGGCHPVSSLPLLVHFLPLLVHFLPLLVYLLPLLGRFLPRLVYLLPLLVHFLPPLMHFL PLLVHFLALLAHFLPLLVHFLALLAHFPAPAGVFPAPAGVLPSPAGALPASAGALLASPGPT

Signal peptide:

amino acids 1-39

N-myristoylation sites.

amino acids 4-10, 109-115, 116-122

Leucine zipper pattern.

amino acids 14-36, 16-38, 17-39, 21-43, 24-46, 28-50, 31-53, 35-57, 38-60, 42-64, 45-67, 49-71, 52-74, 56-78, 59-81, 63-85, 65-87, 66-88

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FIGURE 195

GGCAAGGCGGCGGCGGCGGCGGCGGCGGTGGCGGCGTGGGGAACATCTCGGCAGCCA CCGCGCTTCTCCCGCTGGAGCGGGCGTCCAGCTTGGCTGCCCTCGGTCCTTCCCTGCCACGTT TCGGGTCGCCCTGCACCCCCACCCAGGCTCGCTTCTCTTCGAAGCGGGAAGGGCGCCTTGCA GGATCCTGCCGCCCCTCCAACCGGATCCTGGGTCTAGAGCTCCCCAGAGCGAGGCGCTCGCCA GGACTCCTGCCCCGCCAACCCTGACCGCCGGGGGGTGCCCCCGGGACGTAGCGCCGCGGAGAG GAAGCGGCAAAGGGGACC**ATG**CGGCGCCTGACTCGTCGGCTGGTTCTGCCAGTCTTCGGGGTG CTCTGGATCACGGTGCTGCTTCTTCTGGGTAACCAAGAGGAAGTTGGAGGTGCCGACGGGA CCTGAAGTGCAGACCCCTAAGCCTTCGGACGCTGACTGGGACGACCTGTGGGACCAGTTTGAT GAGCGGCGGTATCTGAATGCCAAAAAGTGGCGCGTTGGTGACGACCCCTATAAGCTGTATGCT TTCAACCAGCGGAGAGTGAGCGGATCTCCAGCAATCGGGCCATCCCGGACACTCGCCATCTG AACGAGGCCCGCTCCACGCTGCTCAGGACCATCCGCAGTGTATTAAACCGCACCCCTACGCAT CTGATCCGGGAAATCATATTAGTGGATGACTTCAGCAATGACCCTGATGACTGTAAACAGCTC ATCAAGTTGCCCAAGGTGAAATGCTTGCGCAATAATGAACGGCAAGGTCTGGTCCGGTCCCGG ATTCGGGGCGCTGACATCGCCCAGGGCACCACTCTGACTTTCCTCGACAGCCACTGTGAGGTG AACAGGGACTGGCTCCAGCCTCTGTTGCACAGGGTCAAAGAGGACTACACGCGGGTGGTGTGC CCTGTGATCGATATCATTAACCTGGACACCTTCACCTACATCGAGTCTGCCTCGGAGCTCAGA GGGGGGTTTGACTGGAGCCTCCACTTCCAGTGGGAGCAGCTCTCCCCAGAGCAGAAGGCTCGG CGCCTGGACCCCACGGAGCCCATCAGGACTCCTATCATAGCTGGAGGGCTCTTCGTGATCGAC AAAGCTTGGTTTGATTACCTGGGGAAATATGATATGGACATGGACATCTGGGGTGGGGAGAAC TTTGAAATCTCCTTCCGAGTGTGGATGTGCGGGGGCAGCCTAGAGATCGTCCCCTGCAGCCGA GTGGGGCACGTCTTCCGGAAGAAGCACCCCTACGTTTTCCCTGATGGAAATGCCAACACGTAT GCCCGCCATTCGCCCTGGAGAGGCCCTTCGGGAATGTTGAGAGCAGATTGGACCTGAGGAAG AATCTGCGCTGCCAGAGCTTCAAGTGGTACCTGGAGAATATCTACCCTGAACTCAGCATCCCC AAGGAGTCCTCCATCCAGAAGGGCAATATCCGACAGAGACAGAAGTGCCTGGAATCTCAAAGG CAGAACAACCAAGAAACCCAAACCTAAAGTTGAGCCCCTGTGCCAAGGTCAAAGGCGAAGAT GCAAAGTCCCAGGTATGGGCCTTCACATACACCCAGCAGATCCTCCAGGAGGAGCTGTGCCTG TCAGTCATCACCTTGTTCCCTGGCGCCCCAGTGGTTCTTGTCCTTTGCAAGAATGGAGATGAC CGACAGCAATGGACCAAAACTGGTTCCCACATCGAGCACATAGCATCCCACCTCTGCCTCGAT ACAGATATGTTCGGTGATGGCACCGAGAACGGCAAGGAAATCGTCGTCAACCCATGTGAGTCC TCACTCATGAGCCAGCACTGGGACATGGTGAGCTCT**TGA**GGACCCCTGCCAGAAGCAGCAAGG CCACCTCAGACATCCTGGACTGGGAGGTGGAGGCAGAGCCCCCCAGGACAGGAGCAACTGTCT CAGGGAGGACAGAGGAAAACATCACAAGCCAATGGGCTCAAAGACAAATCCCACATGTTCTCA AGGCCGTTAAGTTCCAGTCCTGGCCAGTCATTCCCTGATTGGTATCTGGAGACAGAAACCTAA CCTTCTTTTTCACTAGGCCAGGACTACATTGAGAGATGAAGAATGGAGGTTGTTTCCAAAAGA **ААААААААААА**

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FIGURE 196

MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPTGPEVQTPKPSDADWDDLWDQFDERRYLN
AKKWRVGDDPYKLYAFNQRESERISSNRAIPDTRHLRCTLLVYCTDLPPTSIIITFHNEARST
LLRTIRSVLNRTPTHLIREIILVDDFSNDPDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADI
AQGTTLTFLDSHCEVNRDWLQPLLHRVKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWS
LHFQWEQLSPEQKARRLDPTEPIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGENFEISFR
VWMCGGSLEIVPCSRVGHVFRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKQYYYAARPFAL
ERPFGNVESRLDLRKNLRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQRQNNQET
PNLKLSPCAKVKGEDAKSQVWAFTYTQQILQEELCLSVITLFPGAPVVLVLCKNGDDRQQWTK
TGSHIEHIASHLCLDTDMFGDGTENGKEIVVNPCESSLMSQHWDMVSS

Transmembrane domain:

amino acids 475-493

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 2-6

Tyrosine kinase phosphorylation sites.

amino acids 68-75, 401-409

N-myristoylation sites.

amino acids 178-184, 186-192, 192-198, 346-352, 383-389, 526-532

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FIGURE 197

CGTGGCCAGACTCAGTGGGAGTGCGACCCCGCACCACGGAGCGCCACATCGCCGTACACAAGCGGCTTGTGCTGG CCTTCGCTGTGTCCCTCGTGGCATTGCTCGCGGTCACAATGCTCGCTGTGCTCAGCCTGCGCTTCGACGACGACGT GCGGGGCGAGTGCCACGCCAGGCGCCGACGGTGGCCCCTCAGGCTTTCCGGAGCGCGGCGGCGAACGGGAGCCTCC GGACCACGTCGGCCCAGCCGCCGTCGGAGGAGGAGCGGGAGCCGTGGGAGCCGTGGACGCAGCTGCGCCTGTCGG GCCACCTGAAGCCGCTGCACTACAATCTGATGCTCACCGCCTTCATGGAGAACTTCACCTTCTCCGGGGAGGTCA ACGTGGAGATCGCGTGCCGGAACGCCACCCGCTACGTAGTGCTGCACGCTTCCCGAGTGGCGGTGGAGAAAGTGC AGCTGGCCGAGGACCGGGCGTTCGGGGCTGTCCCTGTAGCCGGTTTTTTCCTCTACCCGCAAACCCAGGTCTTAG TGGTGGTGCTGAATAGGACACTGGACGCGCAGAGGAATTACAATCTGAAGATTATCTACAACGCGCTCATCGAGA ${\tt ATGAGCTCCTGGGCTTCTTCCGCAGCTCCTATGTGCTCCACGGGGAGAGAAGATTCCTTGGTGTTACTCAGTTTT}$ CGCCTACACATGCCAGAAAGGCATTTCCTTGTTTTGATGAGCCAATCTACAAGGCTACTTTCAAAATCAGCATCA CGGATCACTTTTCACAGACCCCTCTCATGTCCACATATTATTTAGCCTGGGCAATTTGCAACTTCACATACAGAG AAACTACCACCAAGAGTGGGGTTGTAGTACGATTATATGCAAGACCTGATGCTATCAGAAGAGGATCCGGGGACT ATGCTCTCCATATAACAAAGAGATTAATAGAATTTTATGAAGACTACTTTAAAGTGCCCTATTCCTTGCCAAAAC TAGATCTTTTAGCTGTGCCTAAGCATCCGTATGCTGCTATGGAGAACTGGGGACTAAGTATTTTTGTGGAACAAA GAATACTGCTGGATCCCAGTGTTTCATCTATTTCTTATTTGCTGGATGTCACCATGGTCATTGTTCATGAGATAT TGCATGAAGTGATGCTGCTGGACGGTTTGGCCAGTTCCCATCCAGTATCACAGGAAGTGCTGCAGGCAACAGATA TTGACAGGGTGTTTGACTGGATCGCATATAAAAAGGGTGCTGCTTTAATAAGAATGCTGGCTAATTTTATGGGCC ATTCAGTTTTCCAGAGGGGTTTGCAAGATTATTTAACCATTCATAAGTATGGTAATGCAGCCAGAAATGATCTCT GGAATACATTATCGGAGGCTTTAAAAAGAAATGGGAAATATGTAAATATACAAGAAGTAATGGATCAGTGGACAC TCCAGATGGGTTATCCTGTTATCACCATCTTGGGAAACACAACAGCAGAAAATAGAATAATAATTACCCAACAGC ATTTTATCTATGATATCAGTGCTAAAACTAAAGCACTTAAACTTCAGAATAACAGTTACCTGTGGCAGATTCCAT TAACTATTGTGGTAGGAAATAGAAGCCATGTGTCTTCAGAAGCAATTATTTGGGTGTCTAACAAATCAGAGCACC GATACCTGTCTGAGGAGGAGGTTTTCTTCCTTGGCATGCTGCCAGCCGAGCTCTTTATCCTCTAGATAAATTAC TGGACCGCATGGAAAACTACAACATTTTCAATGAATATATTTTAAAGCAAGTTGCAACAACATATATCAAGCTTG GGTGGCCGAAAAATAATTTTAATGGATCTCTTGTTCAAGCATCCTACCAACATGAAGAACTACGTAGAAGAAGTTA TAATGCTGGCCTGCAGTTTTGGCAACAAGCACTGTCACCAACAGGCATCAACACTTATTTCAGATTGGATTTCCA GCAACAGGAACAGAATACCACTAAATGTTAGAGACATCGTATACTGTACAGGAGTGTCACTACTGGATGAGGATG TCTGGGAATTCATATGGATGAAATTCCATTCCACCACAGCAGTTTCTGAGAAGAAAATATTATTGGAAGCCTTAA CTTGCAGTGATGACAGGAATTTATTAAACAGGCTTCTAAATCTGTCACTGAATTCTGAGGTGGTGCTGGATCAAG ATGCAATTGATGTCATAATCCATGTAGCTCGAAATCCACATGGTCGAGACCTTGCCTGGAAGTTTTTCAGGGATA AATGGAAGATATTAAATACCAGGTATGGAGAAGCATTGTTTATGTATTCCAAACTCATCAGTGGTGTCACAGAAT TTCTTAATACTGAAGGTGAACTCAAAGAGCTCAAGAACTTCATGAAAAACTATGATGGGGTAGCTGCTTCTT TCTCACGAGCTGTGGAAACTGTCGAAGCCAATGTGCGCTGGAAAATGCTTTACCAAGACGAGCTTTTCCAATGGT GCTTTTTGTGGAATGAGGAAAATGTACTACCTAGAAAATGGCCAGATTTTCAGTGTTAACGTGTGGGAGGAATTT TGGGTGTTCCTCTCTAAAGAAACTCTTGCAAGTGAAACTAGCCATGATTGCTTCAGCTGTACATTCCTTGCTGTA CAGGACCAAATATGATAGTGATGCATGTTGATGTTACAGTCAATTTGGAAAAACATATTCAGAATATCTGTGCAT GAAATGATATTCTCAATTTTGGGCAATGTGAGAGGTAAAATAGCCCTTGACATGATGAACATCACTTATTTCAGC ACTTGGATTGTCTGGCAATGATTACTGTGTTGCTAACTCATTTTCTTTGAGTTAAAGCTGTGTATACATTTTAAA AGGCATATAGATAGTGTATGCATATGTACATAGGGAAGCCCCATATGTATATAGTATGTACACTGC ACATGTACAAAGAATGTCTTCAGATCAAAGAAAATTTATCTCTTTTTTATAAACTTAAGGACAGTTGCAAAAGGCT AAAAAAAAA

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FIGURE 198

MGEDDAALRAGSRGLSDPWADSVGVRPRTTERHIAVHKRLVLAFAVSLVALLAVTMLAVLLSL RFDECGASATPGADGGPSGFPERGGNGSLPGSARRNHHAGGDSWQPEAGGVASPGTTSAQPPS EEEREPWEPWTQLRLSGHLKPLHYNLMLTAFMENFTFSGEVNVEIACRNATRYVVLHASRVAV EKVOLAEDRAFGAVPVAGFFLYPOTOVLVVVLNRTLDAORNYNLKIIYNALIENELLGFFRSS YVLHGERRFLGVTOFSPTHARKAFPCFDEPIYKATFKISIKHOATYLSLSNMPVETSVFEEDG WVTDHFSOTPLMSTYYLAWAICNFTYRETTTKSGVVVRLYARPDAIRRGSGDYALHITKRLIE FYEDYFKVPYSLPKLDLLAVPKHPYAAMENWGLSIFVEQRILLDPSVSSISYLLDVTMVIVHE ICHQWFGDLVTPVWWEDVWLKEGFAHYFEFVGTDYLYPGWNMEKQRFLTDVLHEVMLLDGLAS SHPVSOEVLOATDIDRVFDWIAYKKGAALIRMLANFMGHSVFQRGLQDYLTIHKYGNAARNDL WNTLSEALKRNGKYVNIQEVMDQWTLQMGYPVITILGNTTAENRIIITQQHFIYDISAKTKAL KLONNSYLWOIPLTIVVGNRSHVSSEAIIWVSNKSEHHRITYLDKGSWLLGNINQTGYFRVNY DLRNWRLLIDQLIRNHEVLSVSNRAGLIDDAFSLARAGYLPQNIPLEIIRYLSEEKDFLPWHA ASRALY PLDKLLDRMENYNI FNEY ILKQVATTY I KLGWPKNNFNGSLVQASYQHEELRREVIM LACSFGNKHCHOOASTLISDWISSNRNRIPLNVRDIVYCTGVSLLDEDVWEFIWMKFHSTTAV SEKKILLEALTCSDDRNLLNRLLNLSLNSEVVLDQDAIDVIIHVARNPHGRDLAWKFFRDKWK ILNTRYGEALFMYSKLISGVTEFLNTEGELKELKNFMKNYDGVAAASFSRAVETVEANVRWKM LYODELFOWLGKALRH

Transmembrane domain:

amino acids 44-63

N-glycosylation sites.

amino acids 89-93, 160-164, 175-179, 222-226, 338-342, 605-609, 634-638, 649-653, 663-667, 684-688, 800-804, 906-910

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 362-366

Tyrosine kinase phosphorylation site.

amino acids 520-528

N-myristoylation sites.

amino acids 78-84, 87-93, 90-96, 118-124, 501-507, 604-610, 825-831, 987-993

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 437-447

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FIGURE 199

GGCCCGCGGCCTCCTCCCTCGCTCCCGCTTCCCCTTTCTCGCTCACCGCCGCCCTCCTTCCCCAGCTCCCTCGCC ACTCCGCGGGATCTCGCTGTTCCTCGCTCTGCTCCTGGGGAGCCCGGCGGCAGCGCTGGAGCGAGATGCTCTTCC CGAGGGAGATGCTAGCCCTTTGGGTCCTTACCTCCTGCCCTCAGGAGCCCCGGAGAGAGGCAGTCCTGGCAAAGA GCACCCTGAAGAGAGAGTGGTAACAGCGCCCCCCAGTTCCTCACAGTCGGCGGAAGTGCTGGGCGAGCTGGTGCT GCACGCCTTGCCCCCAAGAAGAAACTGCCTTCGCTCAAGCAGGTGAAĆTCTGCCAGGAAGCAGCTGAGGCCCAA CACGGAGAGCCTGGCCCACCGGGGGACCCGGACCCCATCGTGGCCTCCGAGGAGGCATCAGAAGTGCCCCTTTG GCTGGATCGAAAGGAGAGTGCGGTCCCTACAACACCCCGCACCCCTGCAAATCTCCCCCTTCACTTCGCAGCCCTA TGTGGCCCACACACTCCCCCAGAGGCCAGAACCCGGGGAGCCTGGGCCTGACATGGCCCAGGAGGCCCCCCAGGA GGACACCAGCCCCATGGCCCTGATGGACAAAGGTGAGAATGAGCTGACTGGGTCAGCCTCAGAGGAGAGCCAGGA CAACGTGACAGTCTACACTGGCTATGGGGTGGAGCTCCAGGTGAAGAGTGTGAACCTGTCCGATGGGGAACTGCT CTCCATCCGCGGGGTGGACGCCCTACCCTGACCGTCCTGGCCAACCAGACACTCCTGGTGGAGGGGCAGGTAAT CCGAAGCCCCACCACACCATCTCCGTCTACTTCCGGACCTTCCAGGACGACGGCCTTGGGACCTTCCAGCTTCA CTACCAGGCCTTCATGCTGAGCTGCAACTTTCCCCGCCGGCCTGACTCTGGGGATGTCACGGTGATGGACCTGCA $\tt CTCAGGTGGGGTGGCCCACTTTCACTGCCACCTGGGCTATGAGCTCCAGGGCGCTAAGATGCTGACATGCATCAA$ TGCCTCCAAGCCGCACTGGAGCAGCCAGGAGCCCATCTGCTCAGCTCCTTGTGGAGGGGCAGTGCACAATGCCAC CATCGGCCGCGTCTCTCCCCAAGTTACCCTGAAAACACAAATGGGAGCCAATTCTGCATCTGGACGATTGAAGC $\tt CGGGCAGACCAACAAGTCAGCTCTTCTACGACTCCCTTCAAACCGAGAGTGTCCCTTTTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGGGCCTGCTGAGAGTGTCCCTTTTGAGGGGCCTGCTGAGGGCCTGCTGCTGAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCTGCAGGGCCCTGCAGGAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCTGCAGGGCCCCTGCAGGGCCCTGCAGGGCCCAGGGCCCTGCAGGCCCTGCAGGGCCCCTGCAGGGCCCCTGCAGGGCCCCTGCAG$ CGAAGGCAACACCATCCGCATCGAGTTCACGTCCGACCAGGCCCGGGCGGCCTCCACCTTCAACATCCGATTTGA AGCGTTTGAGAAAGGCCACTGCTATGAGCCCTACATCCAGAATGGGAACTTCACTACATCCGACCCGACCTATAA CATTGGGACTATAGTGGAGTTCACCTGCGACCCCGGCCACTCCCTGGAGCAGGGCCCGGCCATCATCGAATGCAT CAATGTGCGGGACCCATACTGGAATGACACAGAGCCCCTGTGCAGAGCCATGTGTGGGGGGAGCTCTCTGCTGT GGCTGGGGTGGTATTGTCCCCAAACTGGCCCGAGCCCTACGTGGAAGGTGAAGATTGTATCTGGAAGATCCACGT GGGAGAAGAGAAACGGATCTTCTTAGATATCCAGTTCCTGAATCTGAGCAACAGTGACATCTTGACCATCTACGA TGGCGACGAGGTCATGCCCCACATCTTGGGGCAGTACCTTGGGAACAGTGGCCCCCAGAAACTGTACTCCTCCAC GCCAGACTTAACCATCCAGTTCCATTCGGACCCTGCTGGCCTCATCTTTGGAAAGGGCCAGGGATTTATCATGAA CTACATAGAGGTATCAAGGAATGACTCCTGCTCGGATTTACCCGAGATCCAGAATGGCTGGAAAACCACTTCTCA ${\tt CACGGAGTTGGTGCGGGGAGCCAGAATCACCTACCAGTGTGACCCCGGCTATGACATCGTGGGGAGTGACACCCT}$ CACCTGCCAGTGGGACCTCAGCTGGAGCAGCGACCCCCATTTTGTGAGAAAATTATGTACTGCACCGACCCCGG AGAGGTGGATCACTCGACCCGCTTAATTTCGGATCCTGTGCTGCTGGTGGGGACCACCATCCAATACACCTGCAA ${\tt CCCCGGTTTTGTGCTTGAAGGGAGTTCTCTTCTGACCTGCTACAGCCGTGAAACAGGGACTCCCATCTGGACGTC}$ TCGCCTGCCCCACTGCGTTTCGGAGGAGTCCCTGGCATGTGACAACCCAGGGCTGCCTGAAAATGGATACCAAAT CCTGTACAAGCGACTCTACCTGCCAGGAGAGTCCCTCACCTTCATGTGCTACGAAGGCTTTGAGCTCATGGGTGA AGTGACCATCCGCTGCATCCTGGGACAGCCATCCCACTGGAACGGGCCCCTGCCCGTGTGTAAAGTTAATCAAGA CAGTTTTGAACATGCTTTAGAAGCAGAAGCGGCAGCAGAGACGTCGCTGGAAGGGGGGAACATGGCCCTGGCTAT CTTCATCCCGGTCCTCATCATCTCCTTACTGCTGGGAGGAGCCTACATTTACATCACAAGATGTCGCTACTATTC CAACCTCCGCCTGCTCTGATGTACTCCCACCCCTACAGCCAGATCACCGTGGAAACCGAGTTTGACAACCCCAT AAAAAAAAA

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FIGURE 200

MPAAR PPAAGLRGISLFLALLLGS PAAALERDAL PEGDAS PLGPYLLPSGAPERGS PGKEHPE ERVVTAPPSSSOSAEVLGELVLDGTAPSAHHDIPALSPLLPEEARPKHALPPKKKLPSLKQVN SARKQLRPKATSAATVQRAGSQPASQGLDLLSSSTEKPGPPGDPDPIVASEEASEVPLWLDRK ESAVPTTPAPLQISPFTSQPYVAHTLPQRPEPGEPGPDMAQEAPQEDTSPMALMDKGENELTG SASEESQETTTSTIITTVITTEQAPALCSVSFSNPEGYIDSSDYPLLPLNNFLECTYNVTVY TGYGVELOVKSVNLSDGELLSIRGVDGPTLTVLANOTLLVEGQVIRSPTNTISVYFRTFQDDG LGTFOLHYOAFMLSCNFPRRPDSGDVTVMDLHSGGVAHFHCHLGYELQGAKMLTCINASKPHW SSQEPICSAPCGGAVHNATIGRVLSPSYPENTNGSQFCIWTIEAPEGQKLHLHFERLLLHDKD RMTVHSGOTNKSALLYDSLOTESVPFEGLLSEGNTIRIEFTSDQARAASTFNIRFEAFEKGHC YEPYIQNGNFTTSDPTYNIGTIVEFTCDPGHSLEQGPAIIECINVRDPYWNDTEPLCRAMCGG ELSAVAGVVLSPNWPEPYVEGEDCIWKIHVGEEKRIFLDIQFLNLSNSDILTIYDGDEVMPHI LGOYLGNSGPOKLYSSTPDLTIOFHSDPAGLIFGKGOGFIMNYIEVSRNDSCSDLPEIQNGWK TTSHTELVRGARITYQCDPGYDIVGSDTLTCQWDLSWSSDPPFCEKIMYCTDPGEVDHSTRLI SDPVLLVGTTIQYTCNPGFVLEGSSLLTCYSRETGTPIWTSRLPHCVSEESLACDNPGLPENG YQILYKRLYLPGESLTFMCYEGFELMGEVTIRCILGQPSHWNGPLPVCKVNQDSFEHALEAEA AAETSLEGGNMALAIFIPVLIISLLLGGAYIYITRCRYYSNLRLPLMYSHPYSQITVETEFDN-PIYETGETREYEVSI

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 893-915

N-glycosylation sites.

amino acids 311-315, 328-332, 350-354, 435-439, 458-462, 474-478, 514-518, 576-580, 618-622, 674-678, 742-746

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 188-192

N-myristoylation sites.

amino acids 23-29, 87-93, 146-152, 454-460, 475-481, 575-581, 629-635, 695-701, 723-729, 766-772, 877-883, 953-959

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 383-394

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FIGURE 201

G<u>ATG</u>GCTACGGCAGGGGGTGGCTCTGGGGCTGACCCGGGAAGTCGGGGTCTCCTTCGCCTTCT CCCCTTAAATAAACAGCTCCCTGTGTTCGCCTGCTCAACGCCACTCATCAGATTGGCTGCCA GTCTTCAATTAGTGGAGACACAGGGGTTATCCACGTAGTAGAGAAAGAGGAGGACCTACAGTG GGATTTAATGGAGAAGCTGAAAGGGAGAACCAGCCGAATTGCTGGTCTTGCAGTGTCCTTGAC CAAGCCCAGTCCTGCCTCAGGCTTCTCCCTAGTGTACAGTGCCCAAATGATGGGTTTGGTGT TTACTCCAATTCCTATGGGCCAGAGTTTGCTCACTGCAGAGAAATACAGTGGAATTCGCTGGG CAAAGTCATCAAGCAGTGCTATCAAGATCACAACCTGAGTCAGAATGGCTCAGCCAACCTT CCCACTATGTGCCATGCAGCTCTTTTCACACATGCATGCTGTCATCAGCACTGCCACCTGCAT GCGGCGCAGCTCCAAAGCACCTTCAGCATCAACCCAGAAATCGTCTGTGACCCCCTGTC TGATTACAATGTGTGGAGCATGCTAAAGCCTATAAATACAACTGGGACATTAAAGCCTGACGA CAGGGTTGTGGTTGCCACCCGGCTGGATAGTCGTTCCTTTTTCTGGAATGTGGCCCCAGG ACCTGATGTGACCACCCTGCCCCGCAATGTCATGTTTTGTCTTTCTAAGGGGAAACTTTTGA CTACATTGGCAGCTCGAGGATGGTCTACGATATGGAGAAGGGCAAGTTTCCCGTGCAGTTAGA GAATGTTGACTCATTTGTGGAGCTGGGACAGGTGGCCTTAAGAACTTCATTAGAGCTTTGGAT GCACACAGATCCTGTTTCTCAGAAAAATGAGTCTGTACGGAACCAGGTGGAGGATCTCCTGGC CACATTGGAGAAGAGTGGTGCTGGTGTCCCTGCTGTCATCCTCAGGAGGCCAAATCAGTCCCA GCCTCTCCCACCATCTTCCCTGCAGCGATTTCTTCGAGCTCGAAACATCTCTGGCGTTGTTCT GGCTGACCACTCTGGTGCCTTCCATAACAAATATTACCAGAGTATTTACGACACTGCTGAGAA CATTAATGTGAGCTATCCCGAATGGCTGAGCCCTGAAGGACCTGAACTTTGTAACAGACAC TGCCAAGGCCCTGGCAGATGTGGCCACGGTGCTGGGACGTGCTCTGTATGAGCTTGCAGGAGG AACCAACTTCAGCGACACAGTTCAGGCTGATCCCCAAACGGTTACCCGCCTGCTCTATGGGTT GGGTGACGGCCTCTTCAACATTACATCGCTGTCTCCAGCCCCACCAACACCACTTATGTTGT ACAGTATGCCTTGGCAAATTTGACTGGCACAGTGGTCAACCTCACCCGAGAGCAGTGCCAGGA TCCAAGTAAAGTCCCAAGTGAAAACAAGGATCTGTATGAGTACTCATGGGTCCAGGGCCCTTT GCATTCTAATGAGACGGACCGACTCCCCCGGTGTGTGCGTTCTACTGCACGATTAGCCAGGGC CTTGTCTCCTGCCTTTGAACTGAGTCAGTGGAGCTCTACTGAATACTCTACATGGACTGAGAG CCGCTGGAAAGATATCCGTGCCCGGATATTTCTCATCGCCAGCAAAGAGCTTGAGTTGATCAC CCTGACAGTGGGCTTCGGCATCCTCATCTTCTCCCTCATCGTCACCTACTGCATCAATGCCAA AGCTGATGTCCTTTTCATTGCTCCCCGGGAGCCAGGAGCTGTGTCATAC**TGA**GGAGGACCCCA GCTTTTCTTGCCAGNTCAGCAGTTCACTTCCTAGAGCATCTGTCCCACTGGGACACAACCACT AATTTGTCACTGGAACCTCCCTGGGCCTGTCTCAGATTGGGATTAACATAAAAGAGTGGAACT ATCCAAAAGAGACAGGGAGAAATAAATAAATTGCCTCCCTTCCTCCGCTCCCCTTTCCCATCA CCCCTTCCCCATTCCTCTTCCTTCTCTACTCATGCCAGATTTTGGGATTACAAATAGAAGCT TCTTGCTCCTGTTTAACTCCCTAGTTACCCACCCTAATTTGCCCTTCAGGACCCTTCTACTTT TTCCTTCCTGCCCTGTACCTCTCTCTCTCTCCTCACCCCCACCCCTGTACCCAGCCACCTTCCT GACTGGGAAGGACATAAAAGGTTTAATGTCAGGGTCAAACTACATTGAGCCCCTGAGGACAGG GGCATCTCTGGGCTGAGCCTACTGTCTCCCTTCCCACTGTCCTTTCTCCAGGCCCTCAGATGGC ACATTAGGGTGGGCGTGCGGGTGGGTATCCCACCTCCAGCCCACAGTGCTCAGTTGTACT TTTTATTAAGCTGTAATATCTATTTTTGTTTTTTGTCTTTTTCCTTTATTCTTTTTTGTAAATAT ATATATAATGAGTTTCATTAAAATAGATTATCCC

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FIGURE 202

MATAGGGSGADPGSRGLLRLLSFCVLLAGLCRGNSVERKIYIPLNKTAPCVRLLNATHQIGCQ SSISGDTGVIHVVEKEEDLQWVLTDGPNPPYMVLLESKHFTRDLMEKLKGRTSRIAGLAVSLT KPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCREIQWNSLGNGLAYEDFSFPIFLLEDENET KVIKQCYQDHNLSQNGSAPTFPLCAMQLFSHMHAVISTATCMRRSSIQSTFSINPEIVCDPLS DYNVWSMLKPINTTGTLKPDDRVVVAATRLDSRSFFWNVAPGAESAVASFVTQLAAAEALQKA PDVTTLPRNVMFVFFQGETFDYIGSSRMVYDMEKGKFPVQLENVDSFVELGQVALRTSLELWM HTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVILRRPNQSQPLPPSSLQRFLRARNISGVVL ADHSGAFHNKYYQSIYDTAENINVSYPEWLSPEEDLNFVTDTAKALADVATVLGRALYELAGG TNFSDTVQADPQTVTRLLYGFLIKANNSWFQSILRQDLRSYLGDGPLQHYIAVSSPTNTTYVV QYALANLTGTVVNLTREQCQDPSKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARA LSPAFELSQWSSTEYSTWTESRWKDIRARIFLIASKELELITLTVGFGILIFSLIVTYCINAK ADVLFIAPREPGAVSY

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 671-692

N-glycosylation sites.

amino acids 45-49, 55-59, 187-191, 200-204, 204-208, 264-268, 387-391, 417-421, 435-439, 464-468, 506-510, 530-534, 562-566, 573-577, 580-584, 612-616

Glycosaminoglycan attachment site.

amino acids 404-408

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 232-236

N-myristoylation site.

amino acids 5-11, 6-12, 9-15, 29-35, 61-67, 120-126, 146-152, 168-174, 205-211, 294-300, 438-444, 446-452, 504-510, 576-582

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FIGURE 203

GCTAGACCGAGCCCTGGGAGGCTACGGGCTCCCCCGGAAACCCTGCCAGGGGAGCCGGGTTTT GAGCTCAGGCGCCTCTAGCGGCGCCCCCAGAAATCTGACTCGCGAGGCCAGAGTTGCAGGGA CTGAATAGCAAACTGAGGCTGAGTAGGGAACAGACC**ATG**AGGTCAGTGCAGATCTTCCTCTCC CAATGCCGTTTGCTCCTTCTACTAGTTCCGACAATGCTCCTTAAGTCTCTTGGCGAAGATGTA ATTTTTCACCCTGAAGGGGAGTTTGACTCGTATGAAGTCACCATTCCTGAGAAGCTGAGCTTC CGGGGAGAGGTGCAGGTCTGCTCCCGTGTCCTACCTACTGCAGTTAAAAAGGCAAGAAG CACGTCCTCCATTTGTGGCCCAAGAGACTTCTGTTGCCCCGACATCTGCGCGTTTTCTCCTTC ACAGAACATGGGGAACTGCTGGAGGATCATCCTTACATACCAAAGGACTGCAACTACATGGGC GTATTTAACATTGATGCCAAACATTACCAAATTGAGCCCCTCAAGGCCTCTCCCAGTTTTGAA CATGTCGTCTATCTCCTGAAGAAGAGCAGTTTGGGGAATCAGGTTTGTGGCTTAAGTGATGAT GAAATAGAATGGCAGATGGCCCCTTATGAGAATAAGGCGAGGCTAAGGGACTTTCCTGGATCC TATAAACACCCAAAGTACTTGGAATTGATCCTACTCTTTGATCAAAGTAGGTATAGGTTTTGTG AACAACAATCTTTCTCAAGTCATACATGATGCCATTCTTTTGACTGGGATTATGGACACCTAC TTTCAAGATGTTCGTATGAGGATACACTTAAAGGCTCTTGAAGTATGGACAGATTTTAACAAA GTATTAAATGCTCGCCTGTCATCAGATTGGGCACATTTATATCTTCAAAGAAAATATAATGAT GCTCTTGCATGGTCGTTTGGAAAAGTGTGTTCTCTAGAATATGCTGGATCAGTGAGTACTTTA CTAGATACAAATATCCTTGCCCCTGCTACCTGGTCTGCTCATGAGCTGGGTCATGCTGTAGGA ATGTCACATGATGAACAATACTGCCAATGTAGGGGTAGGCTTAATTGCATCATGGGCTCAGGA CGCACTGGGTTTAGCAATTGCAGTTATATCTCTTTTTTTAAACATATCTCTTCGGGAGCAACA TGTCTAAATAATATCCCAGGACTAGGTTATGTGCTTAAGAGATGTGGAAACAAAATTGTGGAG GACAATGAGGAATGTGACTGTGGTTCCACAGAGGGGTGTCAGAAAGATCGGTGTTGCCAATCA AATTGTAAGTTGCAACCAGGTGCCAACTGTAGCATTGGACTTTGCTGTCATGATTGTCGGTTT GGGAATTCAAGTTCCTGCCCAAATGACGTTTATAAGCAGGATGGAACCCCTTGCAAGTATGAA GGCCGTTGTTTCAGGAAGGGGTGCAGATCCAGATATATGCAGTGCCAAAGCATTTTTTGGACCT GATGCCATGGAGGCTCCTAGTGAGTGCTATGATGCAGTTAACTTAATAGGTGATCAATTTGGT AACTGTGAGATTACAGGAATTCGAAATTTTAAAAAGTGTGAAAGTGCAAATTCAATATGTGGC AGGCTACAGTGTATAAATGTTGAAACCATCCCTGATTTGCCAGAGCATACGACTATAATTTCT ACTCATTTACAGGCAGAAAATCTCATGTGCTGGGGCACAGGCTATCATCTATCCATGAAACCC ATGGGAATACCTGACCTAGGTATGATAAATGATGGCACCTCCTGTGGAGAAGGCCGGGTATGT TTTAAAAAAATTGCGTCAATAGCTCAGTCCTGCAGTTTGACTGTTTGCCTGAGAAATGCAAT TGTGAGGAAGTGGGGTATGGAGGAAGCATTGACAGTGGGCCTCCAGGACTGCTCAGAGGGGCC ATTCCCTCGTCAATTTGGGTTGTCCCATCATAATGTTTCGCCTTATTTTATTAATCCTTTCA GTGGTTTTTGTGTTTTTCCGGCAAGTGATAGGAAACCACTTAAAACCCAAACAGGAAAAAATG CCACTATCCAAAGCAAAAACTGAACAGGAAGAATCTAAAACAAAAACTGTACAGGAAGAATCT AAAACAAAAACTGGACAGGAAGAATCTGAAGCAAAAACTGGACAGGAAGAATCTAAAGCAAAA ACTGGACAGGAAGAATCTAAAGCAAACATTGAAAGTAAACGACCCAAAGCAAAGAGTGTCAAG GCTAATCATTTATCCAAAGGCTTTCCATTCTTCTCCCAATATTTTTTTACTTTAATTTTTCCC ACAAGTTTTGATCAGCAAATAAACAGCATTCTTGTTTTGGAAACAAAAA

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FIGURE 204

MRSVQIFLSQCRLLLLLVPTMLLKSLGEDVIFHPEGEFDSYEVTIPEKLSFRGEVQGVVSPVS
YLLQLKGKKHVLHLWPKRLLLPRHLRVFSFTEHGELLEDHPYIPKDCNYMGSVKESLDSKATI
STCMGGLRGVFNIDAKHYQIEPLKASPSFEHVVYLLKKEQFGNQVCGLSDDEIEWQMAPYENK
ARLRDFPGSYKHPKYLELILLFDQSRYRFVNNNLSQVIHDAILLTGIMDTYFQDVRMRIHLKA
LEVWTDFNKIRVGYPELAEVLGRFVIYKKSVLNARLSSDWAHLYLQRKYNDALAWSFGKVCSL
EYAGSVSTLLDTNILAPATWSAHELGHAVGMSHDEQYCQCRGRLNCIMGSGRTGFSNCSYISF
FKHISSGATCLNNIPGLGYVLKRCGNKIVEDNEECDCGSTEECQKDRCCQSNCKLQPGANCSI
GLCCHDCRFRPSGYVCRQEGNECDLAEYCDGNSSSCPNDVYKQDGTPCKYEGRCFRKGCRSRY
MQCQSIFGPDAMEAPSECYDAVNLIGDQFGNCEITGIRNFKKCESANSICGRLQCINVETIPD
LPEHTTIISTHLQAENLMCWGTGYHLSMKPMGIPDLGMINDGTSCGEGRVCFKKNCVNSSVLQ
FDCLPEKCNTRGVCNNRKNCHCMYGWAPPFCEEVGYGGSIDSGPPGLLRGAIPSSIWVVSIIM
FRLILLILSVVFVFFRQVIGNHLKPKQEKMPLSKAKTEQEESKTKTVQEESKTKTGQEESEAK
TGQEESKAKTGQEESKANIESKRPKAKSVKKQKK

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 684-705

N-glycosylation sites.

amino acids 222-226, 372-376, 438-442, 473-477, 625-629

N-myristoylation sites.

amino acids 131-137, 168-174, 235-241, 319-325, 364-370, 436-442, 472-478, 609-615, 642-648, 668-674, 676-680, 680-686, 749-755, 758-764, 767-773

Amidation site.

amino acids 69-73

Disintegrins proteins

amino acids 429-479

EGF-like domain proteins

amino acids 650-662

Neutral zinc metallopeptidases, zinc-binding region proteins

amino acids 335-345

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FIGURE 205

CGGACGCGTGGGCGGACGCGTGGGCGGACGCTTGAATGGGGTAGAAGGCCTG AGGGTGACGGGGGCTGGGAAGGGGCAGCTCATGTTCAGGTTTCCAGGAGGGGCTACCTGTTGA CTGTCTTTGCAGGAAGAAAACACCTGAGTGACCAGATGTCCCAGCTCCAGGTGCCTTGCC AGATGGCCAGAACCACCTCTTGAAGAGTGACAGTGCTGTGGAGCATGGTTTCTGCACACCT GGAATGACTGGAACCCCAAAGACTCAAGAAGGAGCTAAAGATCTTGAAGTAGACATGAATAAA ACAGAAGGCTGTGGACCACCTGTCGAGATGGAGAAGTCCTTCTGAGGCTATCCAAACACGGAC ${\tt CAGGCCATGAGACCCCG} {\color{blue} {\bf ATG}} {\tt ACCATCCCTGAATTTTTTCGAGAGTCAGTCAACCGATTTGGAA}$ CTTATCCAGCCCTCCCATCCAAGAATGGCAAAAAGTGGGAAATTCTGAATTTCAACCAGTACT ATGAGGCTTGTCGGAAGGCTGCAAAATCCTTGATCAAGCTGGGTTTGGAGCGTTTCCACGGAG TTGGTATCCTGGGGTTTAACTCTGCAGAGTGGTTTATCACTGCTGTTGGTGCCATCCTAGCCG GGGGTCTTTGTGTTGGTATTTATGCCACCAACTCTGCCGAGGCTTGTCAATATGTCATCACTC ATGCCAAAGTGAACATCTTGCTGGTTGAGAATGATCAACAGTTACAGAAAATCCTTTCGATTC CACAGAGCAGCCTAGAGCCCCTAAAAGCGATCATCCAGTACAGACTGCCAATGAAGAAGAACA ACAACTTGTACTCTTGGGATGATTTCATGGAACTTGGCAGAAGTATCCCTGACACCCAACTGG AGCAGGTCATCGAGAGCCAGAAGGCGAATCAATGCGCAGTGCTCATCTACACTTCAGGGACCA CAGGCATACCCAAGGGAGTGATGCTCAGTCATGACAACATCACGTGGATTGCAGGAGCAGTGA CAAAGGACTTTAAACTGACAGACAAGCATGAGACGGTGGTTAGCTACCTCCCACTCAGCCATA TTGCAGCACAGATGATGGACATCTGGGTACCCATAAAGATTGGGGCGCTCACATACTTTGCTC AAGCAGATGCTCTCAAGGGCACCTTGGTAAGTACTCTAAAGGAGGTAAAACCTACTGTCTTCA TTGGAGTGCCTCAAATTTGGGAGAAGATACATGAGATGGTGAAGAAAAATAGTGCCAAGTCCA TGGGCTTGAAGAAGAAGGCATTCGTGTGGGCAAGAAACATTGGCTTCAAGGTCAACTCAAAAA AGATGTTGGGGAAATATAATACTCCCGTGAGCTACCGCATGGCTAAGACTCTCGTGTTCAGCA AAGTCAAGACATCCCTTGGCTTGGATCACTGTCACTCTTTTATCAGTGGGACTGCGCCCCTCA ACCAAGAGACTGCCGAGTTCTTTCTAAGCTTGGACATACCTATAGGCGAGTTGTATGGGTTGA GTGAGAGCTCGGGACCCCACACGATATCCAACCAGAATAACTACAGGCTTCTAAGCTGTGGCA AGATCTTGACTGGGTGTAAGAATATGCTGTTCCAGCAGAACAAGGATGGCATTGGGGAGATCT GCCTCTGGGGTAGGCACATCTTCATGGGCTATCTGGAAAGTGAGACTGAAACTACAGAGGCCA TCGATGATGAAGGCTGGCTACACTCTGGGGATCTGGGCCAGCTGGACGGTCTGGGTTTCCTCT ATGTCACCGGCCACATCAAAGAAATCCTTATCACTGCTGGTGGTGAAAATGTGCCCCCCATTC CTGTTGAGACCTTGGTTAAGAAGAAGATCCCCATCATCAGTAACGCCATGTTAGTAGGAGATA AACTGAAGTTTCTGAGCATGTTGCTGACGCTGAAGTGTGAGATGAATCAGATGAGCGGAGAAC CTCTGGACAAGCTGAACTTCGAGGCCATCAACTTCTGTCGGGGTCTGGGCAGCCAGGCATCCA CCGTGACTGAGATTGTGAAGCAGCAAGACCCCCTGGTCTACAAGGCCATCCAGCAAGGCATCA ATGCTGTGAACCAGGAAGCCATGAACAATGCACAGAGGATTGAAAAGTGGGTCATCTTGGAGA AGGACTTTTCCATCTATGGTGGAGAGCTAGGTCCAATGATGAAACTTAAGAGACATTTTGTAG CCCAGAAATACAAAAAAAAATTGATCACATGTACCAC<u>TGA</u>CTGCTTTGATGGAGCTGCTCTC AGCTGTTCTGATGCCTTCAGCAGGAAGACCTCATTGCAATAAGTGAAATGCTGCTCTAGGTAG AAGCTCTCCCTGCTGTTTTTAAGAAGCCACATTCCTCATTGGTCAGTTTCTTGATTGTTCGTC TGTTGGAGAGGTGCTCCCTAGAAGAACCTGCCATACGTTTCAAAGCAATAAAATCACTGTATA TCTTTCTAAGGACCTTCAAGTCATGACTCCAGGGAAGCCTATTGGGAAGTCTACTAAAAACTG CCTGATTTACAAGAAGACCTGAACTTGTGGGCTCCCATTTGATTTTTTTCTCCTCAGGGGAC TCAGACATTAGAAAGAAAAGCCTCACAGATTTGAAGAACTGGACCCCCAAATCAACTCACCT GCCTGGAAGCAACTGGGAAACCCTTCCAATAAGTCCTGATAATAAAGCACTTCAGGGTCCCAA AAAAAAAAA

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FIGURE 206

MTIPEFFRESVNRFGTYPALPSKNGKKWEILNFNQYYEACRKAAKSLIKLGLERFHGVGILGF
NSAEWFITAVGAILAGGLCVGIYATNSAEACQYVITHAKVNILLVENDQQLQKILSIPQSSLE
PLKAIIQYRLPMKKNNNLYSWDDFMELGRSIPDTQLEQVIESQKANQCAVLIYTSGTTGIPKG
VMLSHDNITWIAGAVTKDFKLTDKHETVVSYLPLSHIAAQMMDIWVPIKIGALTYFAQADALK
GTLVSTLKEVKPTVFIGVPQIWEKIHEMVKKNSAKSMGLKKKAFVWARNIGFKVNSKKMLGKY
NTPVSYRMAKTLVFSKVKTSLGLDHCHSFISGTAPLNQETAEFFLSLDIPIGELYGLSESSGP
HTISNQNNYRLLSCGKILTGCKNMLFQQNKDGIGEICLWGRHIFMGYLESETETTEAIDDEGW
LHSGDLGQLDGLGFLYVTGHIKEILITAGGENVPPIPVETLVKKKIPIISNAMLVGDKLKFLS
MLLTLKCEMNQMSGEPLDKLNFEAINFCRGLGSQASTVTEIVKQQDPLVYKAIQQGINAVNQE
AMNNAQRIEKWVILEKDFSIYGGELGPMMKLKRHFVAQKYKKQIDHMYH

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 65-86

N-glycosylation site.

amino acids 196-200

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 282-286

Tyrosine kinase phosphorylation sites.

amino acids 547-555, 608-616

N-myristoylation sites.

amino acids 15-21, 74-80, 80-86, 84-90, 185-191, 189-195, 253-259, 337-343, 371-377, 448-454, 536-542

Amidation site.

amino acids 24-28

Putative AMP-binding domain signature.

amino acids 177-189

Putative AMP-binding domain proteins.

amino acids 173-190

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FIGURE 207

CCGTCCGGTCCACCCGCCAGCCCGCACAGCCGCCGCCGCCGAGCGTTTCGTGAGCGGCGCT CCGAGGATCAGGAATGGGGCTTCGGGCGCTGGGCGCTCCGAACCCGGCGCACGTAAGAGCC TGGGAGCGCCCGAGCCGCCCGGCTGCCCGGAGCCCCATCGCCTAGGACCGGGAGATGCTGGAA ATGCAACCGCCTGTTCCCCGAGGAGCCGCTGCCCCCGGGACCCCCTGGCACTGTGCGCACCCT GGTCAGCAGCCCCGGAGAAGACGCCGCCCCCAACGCCCGACCCGCGTGGCCGTGGCAGCGCCC ACGCGAGCCCTCTAGGCGACCGCAGGGCCACAGCAGCTCAGCCGCCGGTGCCCCCTCGGAAAC CTCAGCCGCGGAGGCGCGCAGGCTGCTCTTCGCCTTCACGCTCTCGCTCTCCTGCACTTACC TGTGTTACAGCTTCCTGTGCTGCGACGACCTGGGTCGGAGCCGCCTCCTCGGCGCGCCTC GCTGCCTCCGCGGCCCCAGCGCGGGCGGCCAGAAACTTCTCCAGAAGTCCCGCCCCTGTGATC CTCGCCTCTCCGGTTCCAACCACTCCGGCTCACCCAAGCTGGGTACCAAGCGGTTGCCCCAAG CCCTCATTGTGGGCGTGAAGAAGGGGGGCACCCGGGCCGTGCTGGAGTTTATCCGAGTACACC CGGACGTGCGGCCTTGGGCACGGAACCCCACTTCTTTGACAGGAACTACGGCCGCGGGCTGG ATTGGTACAGGAGCCTGATGCCCAGGACCCTCGAGAGCCAGATCACGCTGGAGAAGACGCCCA GCTACTTTGTCACTCAAGAGGCTCCTCGACGCATCTTCAACATGTCCCGAGACACCAAGCTGA TCGTGGTTGTGCGGAACCCTGTGACCCGTGCCATCTCTGATTACACGCAGACACTCTCCAAGA AGCCCGACATCCCGACCTTTGAGGGCCTCTCCTTCCGCAACCGCACCCTGGGCCTGGTGGACG TGGGGCGAGTCCAGGACTTCCTGGGCATTAAGAGATTCATCACGGACAAGCACTTCTATTTCA ACAAGACCAAAGGATTCCCTTGCTTGAAAAAAAACAGAATCGAGCCTCCTGCCTCGATGCTTGG GCAAATCAAAAGGGAGAACTCATGTACAGATTGATCCTGAAGTGATAGACCAGCTCCGAGAAT TTTATAGACCGTATAATATCAAATTTTATGAAACCGTTGGGCAGGACTTCAGGTGGGAA**TAA**G CCCACGAAAGGAAAGGGCTCTCAAGGGCTCTTCTGCTCATCTCTTCCGTGAGATTTGCTCCCA GACCCTCTGATCTCCCTCCAACAACCCTGGCTCCAGCCCCCTTTCCCAACTTGAGTTGCATC ATCTTGGAACCAGGAAGCCCAGCTAAAGCCAAGAGACCAGAGAGTCCCTGCCACTAGTTTTCA TCAGTCTGTTCAAGCAAAGTTGATCTGCTCCTGGCACGTCCAGTAAATTCCAGAATCATTCTC CTTTCTGCCCATAAAGGGCCTTGGAGAATTGCTTTAAGAAGAGTGAATGTTCCAATGATGATA GATATTATAAGCGATGATGGTTCTGTTGCTATGAACACAGCAGTCGGTCCCTGTCATTGTCCA CCCAGGAGTGGCCTTGTTAATTCCAAGTGGCATGTATCTTCCCTCTGAGCTTCATTTCTTCAA GATGCTCTGGGTGGTGGGATGGGAGACCATCCTCAGCCCTCCTCAGACCTTATCAATTCATTG TAAACCAGTGACTTCAGAGCCTATGGTCTCAACTGTGCTTGAAAAACACTGTCTCTGAAAAACA ACTTTGTGATTCTCCCTGCTCCCTGTGGACAAAAGCACATAATTCTGCTGTTACGGGTACTTT GGCTCTCTCGTGTCCTTAATGCTGGGCTTTTCTCTGTAAGCTGGTTCTGCAGCACAATTCATT AATTAAACTTCTCCCAGTGCAAGAAGGCAGCTGGTGCTGGGGGTGTCTGGGGGGTCAGGGAG GAGGGCAAGGACTACATGGGGCAGAGGCAAGGCGGTGGTGGAGATGAGGAAAGAAGTTCTTCT TGGCAGAAGCTGGGGCAGAAAGATCACATGAGATCTGTGGGGACACCCTCTATCTGAAACATA AGTCTGTGTTCATTCTCTGCTTAGAAATTTTAGATCTGAAGTGCTACACTGAAGGTCCGAAGG TTGATGGGGCATCAGATATCTTTTTGGTTGGCCAGCATGATATTTTGAAATAACTGTCAACAG AAAAAAAAA

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FIGURE 208

MAYRVLGRAGPPQPRRARRLLFAFTLSLSCTYLCYSFLCCCDDLGRSRLLGAPRCLRGPSAGG
QKLLQKSRPCDPSGPTPSEPSAPSAPAAAVPAPRLSGSNHSGSPKLGTKRLPQALIVGVKKGG
TRAVLEFIRVHPDVRALGTEPHFFDRNYGRGLDWYRSLMPRTLESQITLEKTPSYFVTQEAPR
RIFNMSRDTKLIVVVRNPVTRAISDYTQTLSKKPDIPTFEGLSFRNRTLGLVDVSWNAIRIGM
YVLHLESWLQYFPLAQIHFVSGERLITDPAGEMGRVQDFLGIKRFITDKHFYFNKTKGFPCLK
KTESSLLPRCLGKSKGRTHVQIDPEVIDQLREFYRPYNIKFYETVGQDFRWE

Signal peptide:

amino acids 1-33

N-glycosylation sites.

amino acids 102-106, 193-197, 235-239, 306-310

Tyrosine kinase phosphorylation site.

amino acids 296-305

N-myristoylation sites.

amino acids 51-57, 100-106, 121-127, 125-131

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 20-31

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FIGURE 209

CTTTCCTTATCTGTGTGTACTCTTATCTCACTGTTCTATTTTTTCTCCTCATTTATATTAACT CTTTCTTACCTTTTTTCTGAACTTCTAGGCCTTCTCTTTCCAGAACTGGTGGAAGACAAATG AAACGCCAAGATGGTAAGAAACAAGCCGCATTTCTCCTTGGGGAGACTGATAATTTAAAAGG GAGACCACTTACATCCCGAAGCGGACGCGGCAGCTGAAGTCAGGAAACCATGCATCACATTAG CAGGAGCCAACTGCAGACTTTAAACTCCGTTCAACATGTGGATGCGGCAGAGAAATCACTGT CCAGACAAGCCGGGGCAGCTCATAAACTGGTTCATCTGCTCCCTGTGCGTCCCGCGGGTGCGT AAGCTCTGGAGCAGCCGGCGTCCAAGGACCCGGAGAAACCTTCTGCTGGGCACTGCGTGTGCC ATCTACTTGGGCTTCCTGGTGAGCCAGGTGGGGAGGGCCTCTCTCCAGCATGGACAGGCGGCT GAGAAGGGGCCACATCGCAGCCGCGACACCGCCGAGCCATCCTTCCCTGAGATACCCCTGGAT GGTACCCTGGCCCCTCCAGAGTCCCAGGGCAATGGGTCCACTCTGCAGCCCAATGTGGTGTAC ATTACCCTACGCTCCAAGCGCAGCAAGCCGGCCAATATCCGTGGCACCGTGAAGCCCAAGCGC AGGAAAAAGCATGCAGTGGCATCGGCTGCCCCAGGGCAGGAGGCTTTGGTCGGACCATCCCTT CAGCCGCAGGAAGCGGCAAGGGAAGCTGATGCTGTAGCACCTGGGTACGCTCAGGGAGCAAAC CTGGTTAAGATTGGAGAGCGACCCTGGAGGTTGGTGCGGGGTCCGGGAGTGCGAGCCGGGGGC CCAGACTTCCTGCAGCCCAGCTCCAGGGAGAGCAACATTAGGATCTACAGCGAGAGCGCCCCC TCCTGGCTGAGCAAAGATGACATCCGAAGAATGCGACTCTTGGCGGACAGCGCAGTGGCAGGG CTCCGGCCTGTGTCCTCTAGGAGCGGAGCCCGTTTGCTGGTGCTGGAGGGGGGGCGCACCTGGC GTGTTTGCCTTCCACCTAGACAGGATCCTGGGGCTCAACAGGACCCTGCCGTCTGTGAGCAGG AAAGCAGAGTTCATCCAAGATGGCCGCCCATGCCCCATCATTCTTTGGGATGCATCTTTATCT TCAGCAAGTAATGACACCCATTCTTCTGTTAAGCTCACCTGGGGAACTTATCAGCAGTTGCTG AAACAGAAATGCTGGCAGAATGGCCGAGTACCCAAGCCTGAATCAGGTTGTACTGAAATACAT ACAAATTGCTGTGGATTCAGACCTCGCAAGGAAGATGCCTGTGTACAGAATGGATTGAGGCCA AAATGTGATGACCAAGGTTCTGCGGCTCTAGCACACATTATCCAGCGAAAGCATGACCCAAGG CATTTGGTTTTTATAGACAACAAGGGTTTCTTTGACAGGAGTGAAGATAACTTAAACTTCAAA TTGTTAGAAGGCATCAAAGAGTTTCCAGCTTCTGCAGTTTCTGTTTTGAAGAGCCAGCACTTA CGGCAGAAACTTCTTCAGTCTCTGTTTCTTGATAAAGTGTATTGGGAAAGTCAAGGAGGTAGA CAAGGAATTGAAAAGCTTATCGATGTAATAGAACACAGAGCCAAAATTCTTATCACCTATATC AATGCACACGGGGTCAAAGTATTACCTATGAATGAA<u>TGA</u>CAAAAGAATCTTCTGGCTAGGGTG TTAGATATATTTATGCATTTTTGGTTTTGTTTTTAAATCAAGCACATCAACCTCAAGCCCGTT TAGCAATGAGGCAGTGTAGATGAATACGTAAAATAAATGACTTTAACCAAGTAGCTATAAAGG TTATATTTTTCTCTAACATCATGCTATGTGTCAGTCTGAACATCTGACAACAGAAATTTCAGT TATTATTCTAGCTAAGTTTTGAAAACATTTGTCATGCTGTTTAATAGAAAACTGCAAACCAGA GATACTGACTCCATTAATAAACCATATTTTGTGCCGTTTTGACTGTTCTGACCAAATACTAAT GGGAACAATTCTTGACGTTTTTCTGTTGCTGATTGTTAACATAGAGCAGTCTCTACACTACCC TGAGGCAACTCTACATTGGAACACTGAGGCTTACAGCCTGCAAGAGCATCAGAGCTGACCATA CATTTAAACAGAAATGCTGGTTTATTTGCAAAATCACCAGTATATTTTCTATTGTGTCTATAA GGTCCAATTTGTATCTAGTGGCTGAGAAATTAAATAATTCTAAAGTATGAAGTTACCTATCTG AAAATGTACTTACAGAGTATCATTTTAAAATGGATGTCTCTTTAAAAATTTTTGTTACTTTTAC CAACAATGTAATATATTTATGTATATTTTATTAATAATAGTGAATTCCTTAAAAATTTGTTCT ATGTACTTATATTTAATTTGATTTAATGGTTACTGCCCAGATATTGAGAAATGGTTCAAATAT TGAGTGTGTTTCAATAA

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FIGURE 210

MTCPDKPGQLINWFICSLCVPRVRKLWSSRRPRTRRNLLLGTACAIYLGFLVSQVGRASLQHG
QAAEKGPHRSRDTAEPSFPEIPLDGTLAPPESQGNGSTLQPNVVYITLRSKRSKPANIRGTVK
PKRRKKHAVASAAPGQEALVGPSLQPQEAAREADAVAPGYAQGANLVKIGERPWRLVRGPGVR
AGGPDFLQPSSRESNIRIYSESAPSWLSKDDIRRMRLLADSAVAGLRPVSSRSGARLLVLEGG
APGAVLRCGPSPCGLLKQPLDMSEVFAFHLDRILGLNRTLPSVSRKAEFIQDGRPCPIILWDA
SLSSASNDTHSSVKLTWGTYQQLLKQKCWQNGRVPKPESGCTEIHHHEWSKMALFDFLLQIYN
RLDTNCCGFRPRKEDACVQNGLRPKCDDQGSAALAHIIQRKHDPRHLVFIDNKGFFDRSEDNL
NFKLLEGIKEFPASAVSVLKSQHLRQKLLQSLFLDKVYWESQGGRQGIEKLIDVIEHRAKILI
TYINAHGVKVLPMNE

Transmembrane domain:

amino acids 40-56

N-glycosylation sites.

amino acids 98-102, 289-293, 322-326

N-myristoylation sites.

amino acids 8-14, 41-47, 97-103, 187-193, 251-257, 252-258, 287-293, 484-490

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FIGURE 211

GTGGGGTGGTGAGCGCAGCGCCGAGGA<u>TG</u>AGGAGGTGCAACAGCGGCTCCGGGCCGCCGCCGTCGCTGCTGCTGC TGCTGCTGTGGCTGCTCGCGGTTCCCGGCGCTAACGCGGCCCCGCGGTCGGCGCTCTATTCGCCTTCCGACCCGC CCTCCTGGTGCGGCCACTGCATCGCCTTCGCCCCGACGTGGAAGGCGCTGGCCGAAGACGTCAAAGCCTGGAGGC CGGCCCTGTATCTCGCCGCCCTGGACTGTGCTGAGGAGACCAACAGTGCAGTCTGCAGAGACTTCAACATCCCTG GCTTCCCGACTGTGAGGTTCTTCAAGGCCTTTACCAAGAACGGCTCGGGAGCAGTATTTCCAGTGGCTGGTGCTG ACGTGCAGACGCTGCGGGAGAGGCTCATTGACGCCCTGGAGTCCCATCATGACACGTGGCCCCCAGCCTGTCCCC CACTGGAGCCTGCCAAGCTGGAGGAGATTGATGGATTCTTTGCGAGAAATAACGAAGAGTACCTGGCTCTGATCT TTGAAAAGGGAGGCTCCTACCTGGGTAGAGAGGTGGCTCTGGACCTGTCCCAGCACAAAGGCGTGGCGGTGCGCACA GGGTGCTGAACACAGAGGCCAATGTGGTGAGAAAGTTTGGTGTCACCGACTTCCCCTCTTGCTACCTGCTGTTCC GGAATGGCTCTGTCTCCCGAGTCCCCGTGCTCATGGAATCCAGGTCCTTCTATACCGCTTACCTGCAGAGACTCT AATTGGCAGATCGCTCCAAGATCTACATGGCTGACCTGGAATCTGCACTGCACTACATCCTGCGGATAGAAGTGG GCAGGTTCCCGGTCCTGGAAGGGCAGCGCCTGGTGGCCCTGAAAAAGTTTGTGGCAGTGCTGGCCAAGTATTTCC CCTACAGTTTCTTTAAAACTGCCCTGGACGACAGGAAAGAGGGTGCCGTTCTTGCCAAGAAGGTGAACTGGATTG AGGCAGCTCGGCAAAATGTAGACCACTCACAGGAAGCAGCCAAGGCCAAGGAGGTCCTCCCAGCCATCCGAGGCT ACGTGCACTACTTCTTCGGCTGCCGAGACTGCGCTAGCCACTTCGAGCAGATGGCTGCCTCCATGCACCGGG TGGGGAGTCCCAACGCCGCTGTCCTCTGGCTCTGGTCTAGCCACAACAGGGTCAATGCTCGCCTTGCAGGTGCCC TGGATGTGCCCGTGTGGGACGTGGAAGCCACCTCAACTTCCTCAAGGCCCACTTCTCCCCAAGCAACATCATCC $\tt TGGACTTCCCTGCAGCTGGGTCAGCTGCCCGGAGGGATGTGCAGAATGTGGCAGCCGCCCCAGAGCTGGCGATGG$ GAGCCCTGGAGCTGGAAAGCCGGAATTCAACTCTGGACCCTGGGAAGCCTGAGATGATGAAGTCCCCCACAAACA CCACCCCACATGTGCCGGCTGAGGGACCTGAGGCAAGTCGACCCCCGAAGCTGCACCCTGGCCTCAGAGCTGCAC CAGGCCAGGAGCCTCCTGAGCACATGGCAGAGCTTCAGAGGAATGAGCAGGAGCAGCCGCTTGGGCAGTGGCACT TGAGCAAGCGAGACACAGGGGCTGCATTGCTGGCTGAGTCCAGGGCTGAGAAGAACCGCCTCTGGGGCCCTTTGG AGGTCAGGCGCGTGGGCCGCAGCTCCAAGCAGCTGGTCGACATCCCTGAGGGCCAGCTGGAGGCCCGAGCTGGAC ${\tt GGGGCCGAGGCCAGTGCTGCAGGTGCTGGGAGGGGGCTTCTCTTACCTGGACATCAGCCTCTGTGTGGGGCTCT}$ $\tt CTGGCCACCCTGCAGCC\underline{TGA} ACCACCTGGGGAGGGGGGGGGGGGGGGGGGGGGCTGCCATCTCTAGGCACCTCAAGCCC$ $\tt CCTGACCCCATTCCCTCCCACCCCTTGCTCCTTGTCTGGCCTAGAAGTGTGGGAAATTCAGGAAAACGAG$ TTGCTCCAGTGAAGCTTCTTGGGGTTGCTAGGACAGAGAGCTCCTTTGACACAAAAGACAGGAGCAGGGTCCAGG TTCCCCTGCTGTGCAGGGAGGGCAGCCCCGGGCAGTGGGCATAGGGCAGCTCAGTCCCTGGCCTCTTAGCACCAC ATTCCTGTTTTTCAGCTTATTTGAAGTCCTGCCTCATTCTCACTGGAGCCTCAGTCTCTCCTGCTTGGTCTTGGC CCCTCTATGCCTGGCCAGCCTCCAGACCTCCTGGGTTGGGGTTTGGCTTCAGGGTTGGGATTTGGAAGC GGGACCTGACGAGTTGGTGGCATGGGAAGGATGTGGGTCTCTAGTGCCTTGCCCTGGCTTAGCTGCAGGAGAAGA CTTCCAGTGTGCAGAAGTTAGAAGGGTCTGGCGGGGGCAGTGCCTTACACATGCTTGATTCCCACGCTACCCCCT GCCTTGGGAGGTGTGTGGAATAAATTATTTTTGTTAAGGCA

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FIGURE 212

MRRCNSGSGPPPSLLLLLLWLLAVPGANAAPRSALYSPSDPLTLLQADTVRGAVLGSRSAWAV
EFFASWCGHCIAFAPTWKALAEDVKAWRPALYLAALDCAEETNSAVCRDFNIPGFPTVRFFKA
FTKNGSGAVFPVAGADVQTLRERLIDALESHHDTWPPACPPLEPAKLEEIDGFFARNNEEYLA
LIFEKGGSYLGREVALDLSQHKGVAVRRVLNTEANVVRKFGVTDFPSCYLLFRNGSVSRVPVL
MESRSFYTAYLQRLSGLTREAAQTTVAPTTANKIAPTVWKLADRSKIYMADLESALHYILRIE
VGRFPVLEGQRLVALKKFVAVLAKYFPGRPLVQNFLHSVNEWLKRQKRNKIPYSFFKTALDDR
KEGAVLAKKVNWIGCQGSEPHFRGFPCSLWVLFHFLTVQAARQNVDHSQEAAKAKEVLPAIRG
YVHYFFGCRDCASHFEQMAAASMHRVGSPNAAVLWLWSSHNRVNARLAGAPSEDPQFPKVQWP
PRELCSACHNERLDVPVWDVEATLNFLKAHFSPSNIILDFPAAGSAARRDVQNVAAAPELAMG
ALELESRNSTLDPGKPEMMKSPTNTTPHVPAEGPEASRPPKLHPGLRAAPGQEPPEHMAELQR
NEQEQPLGQWHLSKRDTGAALLAESRAEKNRLWGPLEVRRVGRSSKQLVDIPEGQLEARAGRG
RGOWLOVLGGGFSYLDISLCVGLYSLSFMGLLAMYTYFQAKIRALKGHAGHPAA

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 705-728

N-glycosylation sites.

amino acids 130-134, 243-247, 575-579

Glycosaminoglycan attachment site.

amino acids 6-10

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 644-648

N-myristoylation sites.

amino acids 52-58, 56-62, 196-202, 381-387, 392-398, 448-454, 468-474, 684-690, 702-708

Cytochrome c family heme-binding site signature.

amino acids 509-515

Thioredoxin family proteins

amino acids 62-78

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FIGURE 213

GCACGAGGCCGACTTCCAGACCATCTACAACTGCACGGCCTGGAACAGCTTCGGCTCCGACAC TGAGATCATCCGGCTCAAGGAGCAAGGTTCGGAAATGAAGTCGGGAGCCGGGCTGGAAGCAGA GTCTGTGCCG**ATG**GCCGTCATCATTGGGGTGGCCGTAGGAGCTGGTGTGGCCTTCCTCGTCCT TATGGCAACCATCGTGGCGTTCTGCTGTGCCCGTTCCCAGAGAAATCTCAAAGGTGTTGTGTC AGCCAAAAATGATATCCGAGTGGAAATTGTCCACAAGGAACCAGCCTCTGGTCGGGAGGGTGA GGAGCACTCCACCATCAAGCAGCTGATGATGGACCGGGGTGAATTCCAGCAAGACTCAGTCCT GAAACAGCTGGAGGTCCTCAAAGAAGAGGAGAAAGAGTTTCAGAACCTGAAGGACCCCACCAA TGGCTACTACAGCGTCAACACCTTCAAAGAGCACCACTCAACCCCGACCATCTCCCTCTCCAG CTGCCAGCCCGACCTGCGTCCTGCGGGTAAGCAGCGTGTGCCCACAGGCATGTCCTTCACCAA CATCTACAGCACCCTGAGCGGCCAGGGCCGCCTCTACGACTACGGCCAGCGGTTTGTGCTGGG CATGGGCAGCTCGTCCATCGAGCTTTGTGAGCGGGAGTTCCAGAGAGGCTCCCTCAGCGACAG CAGCTCCTTCCTGGACACGCAGTGTGACAGCAGCGTCAGCAGCAGCGGCAAGCAGGATGGCTA TGTGCAGTTCGACAAGGCCAGCAAGGCTTCTGCTTCCTCCCCACCACTCCCAGTCCTCGTC CCAGAACTCTGACCCCAGTCGACCCCTGCAGCGGCGGATGCAGACTCACGTC**TAA**GGATCACA CACCGCGGTGGGGACGGCCAGGGAAGAGGTCAGGGCACGTTCTGGTTGTCCAGGGACGAGG GGTACTTTGCAGAGGACACCAGAATTGGCCACTTCCAGGACAGCCTCCCAGCGCCTCTGCCAC TGCCTTCCTTCGAAGCTCTGATCAAGCACAAATCTGGGTCCCCAGGTGCTGTGTGCCAGAGGT GGGCGGTGGGGAGACAGACAGAGGCTGCGCTGAGTGCGCTGTGCTTAGTGCTGGACACCCG TGTCCCCGGCCCTTTCCTGGAGGCCCCTCTACCACCTGCTCTGCCCACAGGCACAAGTGGCAG CTATAACTCTGCTTTCATGAAACTGCGGTCCACTCTCTGGTCTCTCTGTGGGCTCTACCCCTC ACTGACCACAAGCTCTACCTACCCTGTGCCTGTGCTCCCATACAGCCCTGGGGAGAAGGGGA TGACGTCTTCCCAGCACTGAGCTGCCCCAGAAACCCCGGCTCCCCACTGCTGCTCATAGCCCA GCCGGGAGCCCACCCCCAATTTGTTTGGTGTTTTTGTGTCCATACTCTTGCAGTTCTGTCCTTG GACTTGATGCCGCTGAACTCTGCGGTGGGACCGGTCCCGTCAGAGCCTGGTGTACTGGGGGGGA GGGAGGAGGAGCCTGTGCTGACGGAGCACCTCGCCGGGTGTGCCCCTCCTGGGCTGTG TGACCCCAGCCTCCCACCCACCTCCTGCTTTGTGTACTCCTCCCCTCCCCCTCAGCACAATC GGAGTTCATATAAGAAGTGCGGGAGCTTCTCTGGTCAGGGTTCTCTGAACACTTATGGAGAGA GTGCTTCCTGGGAAGTGTGGCGTTTGAAGGGGCTGGAGGCCAGGTCTTTAAGATGGCGAGACT GCCCTTCTCAGCTGATAAACACAAGAACGGCGATCCTGTCTTCAGTAAGGCTCCACGAGAAGA

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FIGURE 214

MAVIIGVAVGAGVAFLVLMATIVAFCCARSQRNLKGVVSAKNDIRVEIVHKEPASGREGEEHS TIKQLMMDRGEFQQDSVLKQLEVLKEEEKEFQNLKDPTNGYYSVNTFKEHHSTPTISLSSCQP DLRPAGKQRVPTGMSFTNIYSTLSGQGRLYDYGQRFVLGMGSSSIELCEREFQRGSLSDSSSF LDTQCDSSVSSSGKQDGYVQFDKASKASASSSHHSQSSSQNSDPSRPLQRRMQTHV

Signal peptide:

amino acids 1-28

Glycosaminoglycan attachment site.

amino acids 150-154

N-myristoylation sites.

amino acids 6-12, 10-16, 36-42, 139-145, 165-171

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 114-125

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FIGURE 215

CAGCCTTCCTCCCCAGCCTGAGTGACTACTCTATTCCTTGGTCCCTGCTATTGTCGGGGACG ATTGCATGGGCTACGCCAGGAAAGTAGGCTGGGTGACCGCAGGCCTGGTGATTGGGGCTGGCG CCTGCTATTGCATTTATAGACTGACTAGGGGAAGAAAACAGAACAAGGAAAAAATGGCTGAGG GTGGATCTGGGGATGTGATGATGCTGGGGGACTGTTCTGGGGCCAGGTATAATGACTGGTCTG ATGATGATGACAGCAATGAGAGCAAGAGTATAGTATGGTACCCACCTTGGGCTCGGATTG GGACTGAAGCTGGAACCAGAGCTAGGGCCAGGGCAAGGGCCAGGGCTACCCGGGCACGTCGGG CTGTCCAGAAACGGGCTTCCCCCAATTCAGATGATACCGTTTTGTCCCCTCAAGAGCTACAAA AGGTTCTTTGCTTGGTTGAGATGTCTGAAAAGCCTTATATTCTTGAAGCAGCTTTAATTGCTC TGGGTAACAATGCTGCTTATGCATTTAACAGAGATATTATTCGTGATCTGGGTGGTCTCCCAA TTGTCGCAAAGATTCTCAATACTCGGGATCCCATAGTTAAGGAAAAGGCTTTAATTGTCCTGA ATAACTTGAGTGTGAATGCTGAAAATCAGCGCAGGCTTAAAGTATACATGAATCAAGTGTGTG ATGACACAATCACTTCTCGCTTGAACTCATCTGTGCAGCTTGCTGGACTGAGATTGCTTACAA ATATGACTGTTACTAATGAGTATCAGCACATGCTTGCTAATTCCATTTCTGACTTTTTCGTT TATTTTCAGCGGGAAATGAAGAAACCAAACTTCAGGTTCTGAAACTCCTTTTGAATTTGGCTG AAAATCCAGCCATGACTAGGGAACTGCTCAGGGCCCAAGTACCATCTTCACTGGGCTCCCTCT TTAATAAGAAGGAGAACAAAGAAGTTATTCTTAAACTTCTGGTCATATTTGAGAACATAAATG ATAATTTCAAATGGGAAGAAAATGAACCTACTCAGAATCAATTCGGTGAAGGTTCACTTTTTT TCTTTTTAAAAGAATTTCAAGTGTGTGCTGATAAGGTTCTGGGAATAGAAAGTCACCATGATT TTTTGGTGAAAGTAAAAGTTGGAAAATTCATGGCCAAACTTGCTGAACATATGTTCCCAAAGA GCCAGGAA**TAA**CACCTTGATTTTGTAATTTAGAAGCAACACACTTGTAAACTATTCATTTTC TCCACCTTGTTTATATGGTAAAGGAATCCTTTCAGCTGCCAGTTTTGAATAATGAATATCATA TTGTATCATCAATGCTGATATTTAACTGAGTTGGTCTTTAGGTTTAAGATGGATAAATGAATA TCACTACTTGTTCTGAAAACATGTTTGTTGCTTTTTTATCTCGCTGCCTAGATTGAAATATTTT GCTATTTCTTCTGCATAAGTGACAGTGAACCAATTCATCATGAGTAAGCTCCCTTCTGTCATT TTCATTGATTTAATTTGTGTATCATCAATAAAATTGTATGTTAATGCTGGAAAGA

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FIGURE 216

MGYARKVGWVTAGLVIGAGACYCIYRLTRGRKQNKEKMAEGGSGDVDDAGDCSGARYNDWSDD DDDSNESKSIVWYPPWARIGTEAGTRARARARATRARRAVQKRASPNSDDTVLSPQELQKV LCLVEMSEKPYILEAALIALGNNAAYAFNRDIIRDLGGLPIVAKILNTRDPIVKEKALIVLNN LSVNAENQRRLKVYMNQVCDDTITSRLNSSVQLAGLRLLTNMTVTNEYQHMLANSISDFFRLF SAGNEETKLQVLKLLLNLAENPAMTRELLRAQVPSSLGSLFNKKENKEVILKLLVIFENINDN FKWEENEPTONOFGEGSLFFFLKEFQVCADKVLGIESHHDFLVKVKVGKFMAKLAEHMFPKSQE

Signal peptide:

amino acids 1-20

N-glycosylation sites.

amino acids 68-72, 189-193, 217-221, 230-234

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 107-111

N-myristoylation sites.

amino acids 13-19, 17-23, 19-25, 54-60, 83-89, 147-153, 255-261, 290-296

Amidation site.

amino acids 29-33

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FIGURE 217

GAGACACAAAGGCAGGCGGGATGCGGGAGCAGGCAAAGGGAAAGCCGAAAGCCGCGCCCCGGC CGGTGACTGGGTGAAGGCGCCGCGCAGCTTTCCCGACGCCGGCTGTACCCGGACCTCCTGGTC GAGCCTGGCGCGCGCAGCCATCGCCCAACTGGCCACGGAGTACGTGTTCTCGGATT AGATGGTCACGTGCATTGCGGTGGGGCTGCCCCTGCTGCTCATCTCGCTGGCCTTCGCGCAGG CCTTTGTGGATTCATATTGCTGGGCGGCTGTTCAGCAGAAGAACTCACTGCAGAGCGAGTCTG GAAACCTCCCACTGTGGCTGCATAAGTTTTTCCCCTACATCCTGCTGCTCTTTGCGATCCTCC TGTACCTGCCCCGCTGTTCTGGCGTTTCGCAGCTGCTCCTCATATTTGCTCAGACTTGAAGT TTATCATGGAAGAACTTGACAAAGTTTACAACCGTGCAATTAAGGCTGCAAAGAGTGCGCGTG ACCTTGACATGAGAGTGGAGCCTGCTCAGTTCCAGGTGTTACCGAGAACTTAGGGCAAAGTT TGTGGGAGGTATCTGAAAGCCACTTCAAGTACCCAATTGTGGAGCAGTACTTGAAGACAAAGA AAAATTCTAATAATTTAATCATCAAGTACATTAGCTGCCGCCTGCTGACACTCATCATTATAC TGTTAGCGTGTATCTACCTGGGCTATTACTTCAGCCTCTCCTCACTCTCAGACGAGTTTGTGT GCAGCATCAAATCAGGGATCCTGAGAAACGACAGCACCGTGCCCGATCAGTTTCAGTGCAAAC TCATTGCCGTGGGCATCTTCCAGTTGCTCAGTGTCATTAACCTTGTGGTTTATGTCCTGCTGG CTCCCGTGGTTGTCTACACGCTGTTTGTTCCATTCCGACAGAAGACAGATGTTCTCAAAGTGT ACGAAATCCTCCCCACTTTTGATGTTCTGCATTTCAAATCTGAAGGGTACAACGATTTGAGCC TCTACAATCTCTTCTTGGAGGAAAATATAAGTGAGGTCAAGTCATACAAGTGTCTTAAGGTAC TGGAGAATATTAAGAGCAGTGGTCAGGGGATCGACCCAATGCTACTCCTGACAAACCTTGGCA TGATCAAGATGGATGTTGTTGATGGCAAAACTCCCATGTCTGCAGAGATGAGAGAGGAGCAGG GGAACCAGACGCAGAGCTCCAAGGTATGAACATAGACAGTGAAACTAAAGCAAATAATGGAG AGAAGAATGCCCGACAGAGACTTCTGGATTCTTCTTGC**TGA**TGATTTTTTTTTCCTTGAGCTGT AAATCTGTGACTTCTGCGACATGGGATTTAATTTGGCTAAAGCACCCCTGTTGGTTTCACAGC

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FIGURE 218

MAIAQLATEYVFSDFLLKEPTEPKFKGLRLELAVDKMVTCIAVGLPLLLISLAFAQEISIGTQ ISCFSPSSFSWRQAAFVDSYCWAAVQQKNSLQSESGNLPLWLHKFFPYILLLFAILLYLPPLF WRFAAAPHICSDLKFIMEELDKVYNRAIKAAKSARDLDMRDGACSVPGVTENLGQSLWEVSES HFKYPIVEQYLKTKKNSNNLIIKYISCRLLTLIIILLACIYLGYYFSLSSLSDEFVCSIKSGI LRNDSTVPDQFQCKLIAVGIFQLLSVINLVVYVLLAPVVVYTLFVPFRQKTDVLKVYEILPTF DVLHFKSEGYNDLSLYNLFLEENISEVKSYKCLKVLENIKSSGQGIDPMLLLTNLGMIKMDVV DGKTPMSAEMREEQGNQTAELQGMNIDSETKANNGEKNARQRLLDSSC

Transmembrane domains:

amino acids 37-55, 108-126, 216-232, 273-290

N-glycosylation sites.

amino acids 255-259, 338-342, 394-398

Glycosaminoglycan attachment site.

amino acids 357-361

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 203-207

N-myristoylation sites.

amino acids 61-67, 174-180, 251-257, 393-399

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 218-229

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FIGURE 219

CTGTGAGTGACACGCTGAGTGGGGTGAAGGGAA**ATG**CTGGTGAATTTCATTTTGAGGTGTG GTTGTTACCCAAGGGGAACATTGTCCCAAGCTGTTGACGCTCTCTATATCAAAGCAGCATGGC TCAAAGCAACGATTCCAGAAGACCGCATAAAAAATATACGATTATTAAAAAAGAAAACAAAAA AGCAGTTTATGAAAAACTGTCAATTTCAAGAACAGCTTCTGTCCTTCTTCATGGAAGACGTTT TTGGTCAACTGCAATTGCAAGGCTGCAAGAAAATACGCTTTGTGGAGGACTTTCATAGCCTTA GGCAGAAATTGAGCCACTGTATTTCCTGTGCTTCATCAGCTAGAGAGATGAAATCCATTACCA GGATGAAAAGAATATTTTATAGGATTGGAAACAAAGGAATCTACAAAGCCATCAGTGAACTGG ATATTCTTCTTCCTGGATTAAAAAATTATTGGAAAGCAGTCAG**TAA**ACCAAAGCCAAGTACA TTGATTTTACAGTTATTTTGAAATACAATAAGAACTGCTAGAAATATGTTTATAACAGTCTAT TTCTTTTAAAAACTTTTTAACATAATACTGACGGCATGTTAGGTGATTCAGAATAGACAAGAA GGATTTAGTAAATTAACGTTTTGGATATAAGTTGTCACTAATTTGCACATTTTCTGTGTTTTC AAATAATGTTTCCATTCTGAACATGTTTTGTCATTCACAAGTACATTGTGTCAACTTAATTTA GGGGAATGACAGATTTCTGGAATGCAATGTAATGTTACTGAGACTTAAATAGATGTTATGTAT ATGATTGTCTGTTTAAGTGTTTGAAAATTGTTAATTATGCCCAGTGTGAACTTAGTACTTAAC AAAAA

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FIGURE 220

MLVNFILRCGLLLVTLSLAIAKHKQSSFTKSCYPRGTLSQAVDALYIKAAWLKATIPEDRIKN IRLLKKKTKKQFMKNCQFQEQLLSFFMEDVFGQLQLQGCKKIRFVEDFHSLRQKLSHCISCAS SAREMKSITRMKRIFYRIGNKGIYKAISELDILLSWIKKLLESSQ

Signal sequence:

amino acids 1-21

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 68-71

N-myristoylation site.

amino acids 148-153

Interleukin-10 proteins.

amino acids 58-94, 74-102, 128-170

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FIGURE 221

TGCTGCTGCTGTTTTTGGGTCTCAGAGGGCCAAGGCAGCAACAGCCTGTGGTCGCCCCAGGA TGCTGAACCGAATGGTGGGCGGGCAGGACACGCAGGAGGGCGAGTGGCCCTGGCAAGTCAGCA TCCAGCGCAACGGAAGCCACTTCTGCGGGGGCAGCCTCATCGCGGAGCAGTGGGTCCTGACGG CTGCGCACTGCTTCCGCAACACCTCTGAGACGTCCCTGTACCAGGTCCTGCTGGGGGCAAGGC AGCTAGTGCAGCCGGGACCACGCTATGTATGCCCGGGTGAGGCAGGTGGAGAGCAACCCCC TGTACCAGGGCACGGCCTCCAGCGCTGACGTGGCCCTGGTGGAGCTGGAGGCACCAGTGCCCT TCACCAATTACATCCTCCCGTGTGCCTGACCCCTCGGTGATCTTTGAGACGGCCATGA ACTGCTGGGTCACTGGCTGGGGCAGCCCCAGTGAGGAAGACCTCCTGCCCGAACCGCGGATCC TGCAGAAACTCGCTGTGCCCATCATCGACACACCCAAGTGCAACCTGCTCTACAGCAAAGACA CCGAGTTTGGCTACCAACCCAAAACCATCAAGAATGACATGCTGTGCGCCGGCTTCGAGGAGG GCAAGAAGGATGCCTGCAAGGGCGACTCGGGCGGCCCCCTGGTGTGCCTCGTGGGTCAGTCGT GGCTGCAGGCGGGGTGATCAGCTGGGGTGAGGGCTGTGCCCGCCAGAACCGCCCAGGTGTCT ACATCCGTGTCACCGCCCACCACACTGGATCCATCGGATCATCCCCAAACTGCAGTTCCAGC CAGCGAGGTTGGGCGGCCAGAAG**TGA**GACCCCCGGGGCCAGGAGCCCCTTGAGCAGAGCTCTG CACCCAGCCTGCCCGCCCACACCATCCTGCTGGTCCTCCCAGCGCTGCTGTTGCACCTGTGAG CCCCACCAGACTCATTTGTAAATAGCGCTCCTTCCTCCCCTCTCAAATACCCTTATTTTATTT

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FIGURE 222

MRRPAAVPLLLLCFGSQRAKAATACGRPRMLNRMVGGQDTQEGEWPWQVSIQRNGSHFCGGS LIAEQWVLTAAHCFRNTSETSLYQVLLGARQLVQPGPHAMYARVRQVESNPLYQGTASSADVA LVELEAPVPFTNYILPVCLPDPSVIFETGMNCWVTGWGSPSEEDLLPEPRILQKLAVPIIDTP KCNLLYSKDTEFGYQPKTIKNDMLCAGFEEGKKDACKGDSGGPLVCLVGQSWLQAGVISWGEG CARQNRPGVYIRVTAHHNWIHRIIPKLQFQPARLGGQK

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation sites.

amino acids 55-58, 79-82

Casein kinase II phosphorylation sites.

amino acids 121-124, 165-168, 167-170, 248-251

Tyrosine kinase phosphorylation sites.

amino acids 78-86, 197-203

N-myristoylation sites.

amino acids 16-21, 37-42, 56-61, 62-67, 118-123

Amidation site.

amino acids 219-222

Serine proteases, trypsin family, histidine active site.

amino acids 71-76

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FIGURE 223

CAAGATGTGGACAGCTCTTGTGCTCATTTGGATTTTCTCCTTGTCCTTATCTGAAAGCCATGC GGCATCCAACGATCCACGCAACTTTGTCCCTAACAAAATGTGGAAGGGATTAGTCAAGAGGAA TGCATCTGTGGAAACAGTTGATAATAAAACGTCTGAGGATGTAACCATGGCAGCAGCTTCTCC TGTCACATTGACCAAAGGGACTTCGGCAGCCCACCTCAACTCTATGGAAGTCACAACAGAGGA CACAAGCAGGACAGATGTGAGTGAACCAGCAACTTCAGGAGTTGCAGCTGATGGTGACCTC CATTGCTCCCACGGCTGTGGCCTCCAGTACGACTGCGGCCTCCATTACGACTGCGGCCTCCAG TATGACTGTGGCCTCCAGTGCTCCCACGACTGCAGCCTCCAGTACAACTGTGGCCTCCATTGC TCCCACGACTGCAGCCTCCAGTATGACTGCGGCCTCCAGCACTCCCATGACACTTGCACTCCC CAGCACAGCCCTCGCACAAGTGCCAAAGAGCAGCGCGTTGCCAAGAACAGCAACCCTGGCCAC ATTGGCCACACGTGCTCAGACTGTAGCGACCACAGCAAACACAGCAGCCCCATGAGCACTCG TCCAAGTCCTTCCAAGCACATGCCCAGTGACACCGCGGCAAGCCCTGTACCCCCTATGCGTCC CCAAGCACAAGGTCCCATTAGCCAGGTGTCAGTGGACCAGCCTGTGGTTAACACAACAAATAA CACCAAGGCACAAGCCAGGGAGCCAACTGCCAGCCCAGTGCCAGTACCTCACACCAGCCCAAT CCCTGAGATGGAGGCCATGTCCCCCACGACACACCCAAGCCCCATGCCATATACCCAGAGGGC CGCTGGGCCAGGCACATCCCAGGCACCGGAGCAGGTAGAGACTGAAGCCACACCAGGTACTGA GCCCAGCACCCAAGGCCAGTACATGGTGGTCACCACTGAGCCCCTCACCCAGGCCGTGGTAGA CAAAACTCTCCTTCTGGTGGTGCTGTTACTCGGGGTGACCCTTTTCATCACAGTCTTGGTTTT GTTTGCCCTGCAGGCCTATGAGAGCTACAAGAAGAAGACTACACCCAGGTGGACTACTTAAT CAACGGGATGTATGCGGACTCAGAAATG**TGA**GGGGGGGGGGGGCCTGGCGGAGGCCTGGCCC ATTGAGGAGATATGCCAGATGCTTAAACACATTTAATTGCTGTCAGATTAATTCCATGATCAC TAAAGAGTTGCTGCTTTTTTCATATTTATTTTTGTAAATGATTCTGTGCCCAGGAGCAGCTGG GGGTTCCACCTCAGGGTGGGGCGGGCAGGACCCCGTCTCCCCAGGTGTCGGAGCCTGACCTGA ATTAAAGTACTGACTGCTCGCCA

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FIGURE 224

MWTALVLIWIFSLSLSESHAASNDPRNFVPNKMWKGLVKRNASVETVDNKTSEDVTMAAASPV
TLTKGTSAAHLNSMEVTTEDTSRTDVSEPATSGVAADGVTSIAPTAVASSTTAASITTAASSM
TVASSAPTTAASSTTVASIAPTTAASSMTAASSTPMTLALPAPTSTSTGRTPSTTATGHPSLS
TALAQVPKSSALPRTATLATLATRAQTVATTANTSSPMSTRPSPSKHMPSDTAASPVPPMRPQ
AQGPISQVSVDQPVVNTTNKSTPMPSNTTPEPAPTPTVVTTTKAQAREPTASPVPVPHTSPIP
EMEAMSPTTQPSPMPYTQRAAGPGTSQAPEQVETEATPGTDSTGPTPRSSGGTKMPATDSCQP
STQGQYMVVTTEPLTQAVVDKTLLLVVLLLGVTLFITVLVLFALQAYESYKKKDYTQVDYLIN
GMYADSEM

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 396-420

N-glycosylation sites.

amino acids 41-44, 49-52, 222-225, 268-271, 271-274

Casein kinase II phosphorylation sites.

amino acids 14-17, 51-54, 80-83, 85-88, 280-283, 434-437

N-myristoylation sites.

amino acids 68-73, 354-359

Aldo/keto reductase family putative active site signature.

amino acids 195-210

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FIGURE 225

GGAAGGCGCTCAAGGTGCGCGGCCCGGGGCGCGCTACTGGGGGCGCCCTCCGCGGTGGGCAGC GCGCCAGGGATCGGCCTGGGCAGCCGCGGGGCGCGCGAAGGCTGCGCTTTCCCTACGGCCCCC CTCGCTTCCTCCGGCACGGCGCAACGGAGATTTCCTCTCGGGGAAACTACGCGGATCCTTTT CGGGGATCCTCGCCCCGCCCCAGTTCTCCGCCCCCTTCCCCTTTGCTGGGGCGCCTGGGCTGGC GGCCATCGATTCTCCCCGCCATGTGACGCCGTCCTTAGCCCTGCGACCCCCAGCGCGTCCCGG GCCTGCGCCTCCGCCCGCCGCGCGCACGATGCTTCTGCCGGGACGCGCACGCCAACCGC CGACGCCCAGCCCGTGCAGCATCCCGGCCTCCGCCGGCAGGTAGAGCCGCCGGGGCAGCTCC TGCGCCTCTTCTACTGCACTGTCCTGGTCTGCTCCAAAGAGATCTCAGCGCTCACCGACTTCT CTGGTTACCTAACCAAACTCCTGCAAAACCACCACCTATGCCTGTGATGGGGACTATTTGA ATCTACAGTGCCCTCGGCATTCTACGATAAGTGTCCAATCGGCATTTTATGGGCAAGATTACC AAATGTGTAGTTCCCAGAAGCCTGCCTCCCAGAGGGAAGACAGCTTAACCTGTGTGGCAGCCA CCACCTTCCAGAAGGTGCTGGACGAATGCCAGAACCAGCGGGCCTGCCACCTCCTGGTCAATA GCCGTGTTTTTGGACCTGACCTTTGTCCAGGAAGCAGTAAATACCTCCTGGTCTCCTTTAAAT GCCAACCTAATGAATTAAAAAACAAAACCGTGTGTGAAGACCAGGAGCTGAAACTGCACTGCC ATGAATCCAAGTTCCTCAACATCTACTCTGCGACCTACGGCAGGAGGACCCAGGAAAGGGACA TCTGCTCCTCCAAGGCAGAGCGGCTCCCCCTTTCGATTGCTTGTCTTACTCAGCTTTGCAAG TCCTATCCCGAAGGTGCTATGGGAAGCAGAGATGCAAAATCATCGTCAACAATCACCATTTTG GAAGCCCCTGTTTGCCAGGCGTGAAAAAATACCTCACTGTGACCTACGCATGTGTTCCCAAGA ACATACTCACAGCGATTGATCCAGCCATTGCTAATCTAAAACCTTCTTTGAAGCAGAAAGATG GTGAATATGGTATAAACTTCGACCCAAGCGGATCGAAGGTTCTGAGGAAAGATGGAATTCTTG TCGTGTCCAGTGTCTGCATCGGCCTGGCCCTCACACTGTGCGCCCTGGTCATCAGAGAGTCCT GTGCCAAGGACTTCCGCGACTTGCAGCTGGGGAGGGAGCAGCTGGTGCCAGGAAGTGACAAGG TCGAGGAGGACAGCGAGGATGAAGAAGAGGAGGACCCCTCTGAGTCTGATTTCCCAGGGG AACTGTCGGGGTTCTGTAGGACTTCATATCCTATATACAGTTCCATAGAAGCTGCAGAGCTCG CAGAAAGGATTGAGCGCAGGGAGCAAATCATTCAGGAAATATGGATGAACAGTGGTTTGGACA CCTCGCTCCCAAGAAACATGGGCCAGTTCTAC**TGA**AAACCACATGCATCTTGATGCGATCGCA CTTTCTGAAGAAGGAAGGATCCCAAATGCCCCTCCAGTTCTGGTTCACCTGTACCTTCTATGA AGGAGAATTCGTCATGTCATTCAACACTCGTGAGGCCAGGAAGCTATTAAAGGGATGTTTCAA AAAAAAAAAAAAA

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FIGURE 226

MLLPGRARQPPTPQPVQHPGLRRQVEPPGQLLRLFYCTVLVCSKEISALTDFSGYLTKLLQNH
TTYACDGDYLNLQCPRHSTISVQSAFYGQDYQMCSSQKPASQREDSLTCVAATTFQKVLDECQ
NQRACHLLVNSRVFGPDLCPGSSKYLLVSFKCQPNELKNKTVCEDQELKLHCHESKFLNIYSA
TYGRRTQERDICSSKAERLPPFDCLSYSALQVLSRRCYGKQRCKIIVNNHHFGSPCLPGVKKY
LTVTYACVPKNILTAIDPAIANLKPSLKQKDGEYGINFDPSGSKVLRKDGILVSNSLAAFAYI
RAHPERAALLFVSSVCIGLALTLCALVIRESCAKDFRDLQLGREQLVPGSDKVEEDSEDEEEE
EDPSESDFPGELSGFCRTSYPIYSSIEAAELAERIERREQIIQEIWMNSGLDTSLPRNMGQFY

Transmembrane domains:

amino acids 32-49, 322-343

N-glycosylation sites.

amino acids 62-66, 165-169

Tyrosine kinase phosphorylation site.

amino acids 280-287

N-myristoylation site.

amino acids 302-308, 333-339, 428-434

Amidation site.

amino acids 191-195

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FIGURE 227

GGCACGAGGTGGAAGGCTTTTACAAACAGATTGCTGGCCCCACCCCCAGAATTTCTCATCA
GGAGTGGGCAAGACCAATCATTTGCATTTCTGACAAGTTCCCAGGAGCTGCAGCTGCTGGCCC
TGGAACCACACTTTGAGAACCACTGCTTTAGACCAAACACCAAAGGAAGATGCAGCCACCCTC
CTTTACATGTCACAACGCTCAGGGTCCATGAGTACCTCAGGCTGTCCAGCTGAGCTCCACCTG
CAGCAGCCGAGATTCCCGACTCGCTCCACCATTGGGGGGCTAGGAGTGAAGCGTGTCACCATGG
TCAGCTCATGGCCAGCCAGGAAAGCCTCTCTGCTGTGCGTCTGTGCAGTTCTTGTTCTTCCCT
GGAGGACTCTTGGATCGCCTGTGATCTTGGCCAGGAGACCAGGTGCCTGGGTCCCTTCCTGGA
AGGGGACAAGTTACACACCCCAGCCCCATTTTCCCACCAACTTCTACATGCCTTGGGAGAACC
TTCTACATGTTGGCTGCCCCCTTCCCCTATTTCAGCAGTGCCCAGTCCTGCTTATAAACCTGA
GGCCTGCTCCCCATACCTTCCCTGTGCAAGTGCCAGCCGTTATTCCAGGCAGCCCAATGTTGT
TGAGGCCAGATGGATTCCTGGAAGCAGCTGGCCCATGGATGTGTTCTACAAGTATTCTAGA
AACAGAGAAGAGGTCTTAACCTAATGCGCATAGAGAAATTGTTCTCATTGTAAACATACCCCT
GTCCTTAGCTGATCTAGGTGGAAGCCCAGCTTCATGTGCTAGGGGGCCATGATAATGATAATAA
AGGAATTGTATCTAGGACTAA

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FIGURE 228

MVSSWPARKASLLCVCAVLVLPWRTLGSPVILARRPGAWVPSWKGTSYTPQPHFPTNFYMPWE NLLHVGCPLPLFQQCPVLLINLRPAPHTFPVQVPAVIPGSPMLLRPDGFLEAAGPWM

Signal peptide:

amino acids 1-27

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 8-12

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FIGURE 229

GGGAAGGGATGCAAGGAAGCCCTCCGGCGCTCCGAGGCGGGAGACAGCGTCCCGCTGA AAATGTGTGTCTGACATGCAAGCTCAGTGGGGCAGAGACCCGTGGATTGCTGTGCCCTGCCCT CCGGACCTGGATCATGAAGGTGTTGGGAAGAAGCTTCTTCTGGGTGCTGTTTCCCGTCCTTCC CTGGGCGGTGCAGGCTGTGGAGCACGAGGAGGTGGCGCAGCGTGTGATCAAACTGCACCGCGG GCGAGGGGTGCCTGCCATGCAGAGCCGGCAGTGGGTCCGGGACAGCTGCAGGAAGCTCTCAGG GCTTCTCCGCCAGAAGAATGCAGTTCTGAACAAACTGAAAACTGCAATTGGAGCAGTGGAGAA AGACGTGGGCCTGTCGGATGAAGAGAAACTGTTTCAGGTGCACACGTTTGAAATTTTCCAGAA AGAGCTGAATGAAAGTGAAAATTCCGTTTTCCAAGCTGTCTACGGACTGCAGAGAGCCCTGCA GGGGGATTACAAAGATGTCGTGAACATGAAGGAGAGCAGCCGGCAGCGCCTGGAGGCCCTGAG AGAGGCTGCAATAAAGGAAGAAACAGAATATATGGAACTTCTGGCAGCAGAAAAACATCAAGT TGAAGCCCTTAAAAATATGCAACATCAAAACCAAAGTTTATCCATGCTTGACGAGATTCTTGA AGATGTAAGAAAGGCAGCGGATCGTCTGGAGGAAGAGATAGAGGAACATGCTTTTGACGACAA TAAATCAGTCAAGGGGGTCAATTTTGAGGCAGTTCTGAGGGTGGAGGAAGAAGAGGCCAATTC TAAGCAAAATATAACAAAACGAGAAGTGGAGGATGACTTGGGTCTTAGCATGCTGATTGACTC CCAGAACAACCAGTATATTTTGACCAAGCCCAGAGATTCAACCATCCCACGTGCAGATCACCA CATAGGATTGCCTACAATGTTTGGTTATATTATTTGTGGTGTACTTCTGGGACCTTCAGGACT AAATAGTATTAAGTCTATTGTGCAAGTGGAGACATTAGGAGAATTTGGGGTGTTTTTTACTCT TTTTCTTGTTGGCTTAGAATTTTCTCCAGAAAAGCTAAGAAAGGTGTGGAAGATTTCCTTACA AGGGCCGTGTTACATGACACTGTTAATGATTGCATTTGGCTTGCTGTGGGGGCATCTCTTGCG GTCCAGGTTCCTCATGGGCAGTGCTCGGGGTGACAAAGAAGGCGACATTGACTACAGCACCGT GCTCCTCGGCATGCTGGTGACGCAGGACGTGCAGCTCGGGCTCTTCATGGCCGTCATGCCGAC TCTCATACAGGCGGCCCCAGTGCATCTTCTAGCATTGTCGTGGAAGTTCTCCGAATCCTGGT TTTGATTGGTCAGATTCTTTTTTCACTAGCGGCGGTTTTTCTTTTATGTCTTGTTATAAAGAA GTATCTCATTGGACCCTATTATCGGAAGCTGCACATGGAAAGCAAGGGGAACAAAGAAATCCT GATCTTGGGAATATCTGCCTTTATCTTCTTAATGTTAACGGTCACGGAGCTGCTGGACGTCTC GGAGATCGCCACCTCCATCGAACCCATCCGCGACTTCCTGGCCATCGTTTTCTTCGCCTCCAT AGGGCTCCACGTGTTCCCCACGTTTGTGGCGTACGAGCTCACGGTGCTGGTGTTCCTCACCTT GTCAGTGGTGGTGATGAAGTTTCTCCTGGCGGCGCTGGTCCTGTCTCATTCTGCCGAGGAG CAGCCAGTACATCAAGTGGATCGTCTCTGCGGGGCTTGCCCAGGTCAGCGAGTTTTCCTTTGT CCTGGGGAGCCGGGCGCGAAGAGCGGGCGTCATCTCTCGGGAGGTGTACCTCCTTATACTGAG TGTGACCACGCTCAGCCTCTTGCTCGCCCCGGTGCTGTGGAGAGCTGCAATCACGAGGTGTGT ${\tt GCCCAGACCGGAGAGACGGTCCAGCCTC}$ CGTCTGTGGGGAGTGAGCGCTTAGATGGCCAGCAGCTGCTCCTTCTGGGAAGCTCGCACCTTG GCAACAGAACAGCCCTCTAGCAGAGCGTCAGTGCAGTCGTGTTATCCCGGCTTTTACAGAATA TTCTTGTCCTATTTTAGAATTTTCCGGAGTAGTTTATTTGCAGTCTGTTGATTATGTGCAGTA TTTCCCTGAAATTATTATTAATTTTCTATTGTGAGTTCATCAGTTCATAGTTTTTTTAGTAAA GAAGCAAAATTAAAAGGCTTTTAAAAATGTACAACTTCAGAATTATAATCTGTTAGTCAAATA TTTGTTATTAAACATTTCTGTAATATGAAGTTGTAATCCTGGCCGTGAGCTTGGAAGCTTACT TTTGATTCTTAAAGCCTATGTTTTCTAAAATGAGACAAATACGGATGTCTATTTGCCTTTTAT TGTAACTTTTAAATGAAATAATTTCATGTCAATTTCTATTAGATATATCACTTAAAATATTTG

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FIGURE 230

MKVLGRSFFWVLFPVLPWAVQAVEHEEVAQRVIKLHRGRGVAAMQSRQWVRDSCRKLSGLLRQ KNAVLNKLKTAIGAVEKDVGLSDEEKLFQVHTFEIFQKELNESENSVFQAVYGLQRALQGDYK DVVNMKESSRQRLEALREAAIKEETEYMELLAAEKHQVEALKNMQHQNQSLSMLDEILEDVRK AADRLEEEIEEHAFDDNKSVKGVNFEAVLRVEEEEANSKQNITKREVEDDLGLSMLIDSQNNQ YILTKPRDSTIPRADHHFIKDIVTIGMLSLPCGWLCTAIGLPTMFGYIICGVLLGPSGLNSIK SIVQVETLGEFGVFFTLFLVGLEFSPEKLRKVWKISLQGPCYMTLLMIAFGLLWGHLLRIKPT QSVFISTCLSLSSTPLVSRFLMGSARGDKEGDIDYSTVLLGMLVTQDVQLGLFMAVMPTLIQA GASASSSIVVEVLRILVLIGQILFSLAAVFLLCLVIKKYLIGPYYRKLHMESKGNKEILILGI SAFIFLMLTVTELLDVSMELGCFLAGALVSSQGPVVTEEIATSIEPIRDFLAIVFFASIGLHV FPTFVAYELTVLVFLTLSVVVMKFLLAALVLSLILPRSSQYIKWIVSAGLAQVSEFSFVLGSR ARRAGVISREVYLLILSVTTLSLLLAPVLWRAAITRCVPRPERRSSL

Signal peptide:

amino acids 1-22

Transmembrane domains:

amino acids 282-304, 322-337, 354-370, 379-395, 445-474, 501-520, 576-598, 641-660

N-glycosylation sites.

amino acids 104-108, 174-178, 206-210, 230-234

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 55-59, 673-677

Tyrosine kinase phosphorylation site.

amino acids 407-414

N-myristoylation sites.

amino acids 116-122, 327-333, 366-372, 401-407, 419-425, 429-435, 442-448, 525-531, 530-536

Cell attachment sequence.

amino acids 404-407

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FIGURE 231

GAGAAAACAACAGGAAGCAGCTTACAAACTCGGTGAACAACTGAGGGAACCAAACCAGAGAC GCGCTGAACAGAGAGAATCAGGCTCAAAGCAAGTGGAAGTGGGCAGAGATTCCACCAGGACTG GTGCAAGGCGCAGACCAGCCAGATTTGAGAAGAAGCCAAAAAGATGCTGGGGAGCAGAGCTG TAATGCTGCTGCTGCCCTGGACAGCTCAGGGCAGAGCTGTGCCTGGGGGCAGCCC CTGCCTGGACTCAGTGCCAGCAGCTTTCACAGAAGCTCTGCACACTGGCCTGGAGTGCACATC CACTAGTGGGACACATGGATCTAAGAGAGAGGGGAGATGAAGAGACTACAAATGATGTTCCCC AAAGGATCCACCAGGGTCTGATTTTTTATGAGAAGCTGCTAGGATCGGATATTTTCACAGGGG AGCCTTCTCTGCTCCCTGATAGCCCTGTGGGCCAGCTTCATGCCTCCCTACTGGGCCTCAGCC AACTCCTGCAGCCTGAGGGTCACCACTGGGAGACTCAGCAGATTCCAAGCCTCAGTCCCAGCC AGCCATGGCAGCGTCTCCTTCTCCGCTTCAAAATCCTTCGCAGCCTCCAGGCCTTTGTGGCTG TAGCCGCCCGGGTCTTTGCCCATGGAGCAGCAACCCTGAGTCCCTAAAGGCAGCAGCTCAAGG ATGGCACTCAGATCTCCATGGCCCAGCAAGGCCAAGATAAATCTACCACCCCAGGCACCTGTG AGCCAACAGGTTAATTAGTCCATTAATTTTAGTGGGACCTGCATATGTTGAAAATTACCAATA

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FIGURE 232

MLGSRAVMLLLLLPWTAQGRAVPGGSSPAWTQCQQLSQKLCTLAWSAHPLVGHMDLREEGDEE TTNDVPHIQCGDGCDPQGLRDNSQFCLQRIHQGLIFYEKLLGSDIFTGEPSLLPDSPVGQLHA SLLGLSQLLQPEGHHWETQQIPSLSPSQPWQRLLLRFKILRSLQAFVAVAARVFAHGAATLSP

Important features of the protein:

Signal peptide:

amino acids 1-21

Casein kinase II phosphorylation site.

amino acids 64-67

N-myristoylation sites.

amino acids 25-30, 81-86, 122-127

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FIGURE 233

 $\tt CATTAATGGGCCGCTGACATGAATATGGAGTAGTTTTCTCTAGCAAAGAGTA\underline{ATG} TGGGCCATGGAGTCAGGCCA$ CCTCCTCTGGGCTCTGCTGTTCATGCAGTCCTTGTGGCCTCAACTGATGGAGCCACTCGAGTCTACTACCT GGGCATCCGGGATGTGCAGTGGAACTATGCTCCCAAGGGAAGAAATGTCATCACGAACCAGCCTCTGGACAGTGA CATAGTGGCTTCCAGCTTCTTAAAGTCTGACAAGAACCGGATAGGGGGAACCTACAAGAAGACCATCTATAAAGA ATACAAGGATGACTCATACACAGATGAAGTGGCCCAGCCTGCTTGGGCTTCCTGGGGCCAGTGTTGCAGGC TGAAGTGGGGGATGTCATTCTTATTCACCTGAAGAATTTTGCCACTCGTCCCTATACCATCCACCCTCATGGTGT CTTCTACGAGAAGGACTCTGAAGGTTCCCTATACCCAGATGGCTCCTCTGGGCCACTGAAAGCTGATGACTCTGT CCTCACCTGGATCTACCATTCTCATGTAGATGCTCCACGAGACATTGCAACTGGCCTAATTGGGCCTCTCATCAC $\tt CTGTAAAAGAGGAGCCCTGGATGGGAACTCCCCTCCTCAACGCCAGGATGTAGACCATGATTTCTTCCTCCTCTTT$ ${\tt CAGTGTGGTAGATGAGAACCTCAGCTGGCATCTCAATGAGAACATTGCCACTTACTGCTCAGATCCTGCTTCAGT}$ TGAGCTGAACATGTGTGCACAGAAACGTGTGGCCTGGCACTTGTTTGGCATGGGCAATGAAATTGATGTCCACAC AGCATTTTTCCATGGACAGATGCTGACTACCCGTGGACACCACACTGATGTGGCTAACATCTTTCCAGCCACCTT TGTGACTGCTGAGATGGTGCCCTGGGAACCTGGTACCTGGTTAATTAGCTGCCAAGTGAACAGTCACTTTCGAGA TGGCATGCAGGCACTCTACAAGGTCAAGTCTTGCTCCATGGCCCCTCCTGTGGACCTGCTCACAGGCAAAGTTCG ACAGTACTTCATTGAGGCCCATGAGATTCAATGGGACTATGGCCCGATGGGGCATGATGGGAGTACTGGGAAGAA TTTGAGAGAGCCAGGCAGTATCTCAGATAAGTTTTTCCAGAAGAGCTCCAGCCGAATTGGGGGCACTTACTGGAA AGTGCGATATGAAGCCTTTCAAGATGAGACATTCCAAGAGAAGATGCATTTGGAGGAAGATAGGCATCTTGGAAT CCTGGGGCCAGTGATCCGGGCTGAGGTGGGTGACACCATTCAGGTGGTCTTCTACAACCGTGCCTCCCAGCCATT CAGCATGCAGCCCCATGGGGTCTTTTATGAGAAAGACTATGAAGGCACTGTGTACAATGATGGCTCATCTTACCC TGGCTTGGTTGCCAAGCCCTTTGAGAAAGTAACATACCGCTGGACAGTCCCCCCTCATGCCGGTCCCACTGCTCA GGATCCTGCTTGTCTCACTTGGATGTACTTCTCTGCTGCAGATCCCATAAGAGACACAAATTCTGGCCTGGTGGG TCTCTTCACTGTGTTGGATGAGAACAAGAGCTGGTACAGCAATGCCAATCAAGCAGCTGCTATGTTGGATTTCCG CCTGCCCAGGCTGGACATGTGCAAGGGTGACACAGTGGCCTGGCACCTGCTCGGCCTGGGCACAGAGACTGATGT GCATGGAGTCATGTTCCAGGGCAACACTGTGCAGCTTCAGGGCATGAGGAAGGGTGCAGCTATGCTCTTTCCTCA AGAAGCAGGGATGAGGGCAATCTATAATGTCTCCCAGTGTCCTGGCCACCAAGCCACCCCTCGCCAACGCTACCA AGCTGCAAGAATCTACTATATCATGGCAGAAGAAGTAGAGTGGGACTATTGCCCTGACCGGAGCTGGGAACGGGA ATGGCACAACCAGTCTGAGAAGGACAGTTATGGTTACATTTTCCTGAGCAACAAGGATGGGCTCCTGGGTTCCAG ATACAAGAAAGCTGTATTCAGGGAATACACTGATGGTACATTCAGGATCCCTCGGCCAAGGACTGGACCAGAAGA ACACTTGGGAATCTTGGGTCCACTTATCAAAGGTGAAGTTGGTGATATCCTGACTGTGGTATTCAAGAATAATGC CAGCCGCCCTACTCTGTGCATGCTCATGGAGTGCTAGAATCTACTGTCTGGCCACTGGCTGAGCCTGG TGAGGTGGTCACTTATCAGTGGAACATCCCAGAGAGGTCTGGCCCTGGGCCCAATGAGTCTGCTTGTTTTCCTG GATCTATTATTCTGCAGTGGATCCCATCAAGGACATGTATAGTGGCCTGGTGGGGCCCTTGGCTATCTGCCAAAA GGGCATCCTGGAGCCCCATGGAGGACGGAGTGACATGGATCGGGAATTTGCATTGTTGTTCTTGATTTTTGATGA AAATAAGTCTTGGTATTTGGAGGAAAATGTGGCAACCCATGGGTCCCAGGATCCAGGCAGTATTAACCTACAGGA GTACCAAGGAGAACGAGTGGCCTGGTACATGCTGGCCATGGGCCAAGATGTGGATCTACACACCATCCACTTTCA TGCAGAGAGCTTCCTCTATCGGAATGGCGAGAACTACCGGGCAGATGTGGTGGATCTGTTCCCAGGGACTTTTGA AAAAGTGCCCCCAGAGACATTGAAGAAGGCAATGTGAAGATGCTGGGCATGCAGATCCCCATAAAGAATGTTGA ${\tt GATGCTGGCCTCTGTTTTGGTTGCCATTAGTGTCACCCTTCTGCTCGTTGTTCTGGCTCTTTGGTGGAGTGGTTTG}$ GTACCAACATCGACAGAGAAAGCTACGACGCAATAGGAGGTCCATCCTGGATGACAGCTTCAAGCTTCTGTCTTT ${\tt AGTCACTAACCCCACACTCAAAGGGGCATGGGTGGTGGAGAAGCAGAAGGAGCAATCAAGCTTATCTGGATATTT}$ CTTTCTTTATTTTACATGGAAATAATATGATTTCACTTTTTCTTTAGTTTCTTTGCTCTACGTGGGCACCT GGCACTAAGGGAGTACCTTATTATCCTACATCGCAAATTTCAACAGCTACATTATATTTCCTTCTGACACTTGGA ACTTCTTTCAAGGACTCAGGAAATTTCACTTTGAACTGAGGCCAAGTGAGCTGTTAAGATAACCCACACTTAAAC ${\tt TAAAGGCTAAGAATATAGGCTTGATGGGAAATTGAAGGTAGGCTGAGTATTGGGAATCCAAATTGAATTTTGATT}$ CTCCTTGGCAGTGAACTACTTTGAAGAAGTGGTCAATGGGTTGTTGCTGCCATGAGCATGTACAACCTCTGGAGC TAGAAGCTCCTCAGGAAAGCCAGTTCTCCAAGTTCTTAACCTGTGGCACTGAAAGGAATGTTGAGTTACCTCTTC

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FIGURE 234

MWAMESGHLLWALLFMQSLWPQLTDGATRVYYLGIRDVQWNYAPKGRNVITNQPLDSDIVASS FLKSDKNRIGGTYKKTIYKEYKDDSYTDEVAOPAWLGFLGPVLQAEVGDVILIHLKNFATRPY TIHPHGVFYEKDSEGSLYPDGSSGPLKADDSVPPGGSHIYNWTIPEGHAPTDADPACLTWIYH SHVDAPRDIATGLIGPLITCKRGALDGNSPPQRQDVDHDFFLLFSVVDENLSWHLNENIATYC SDPASVDKEDETFOESNRMHAINGFVFGNLPELNMCAOKRVAWHLFGMGNEIDVHTAFFHGQM LTTRGHHTDVANIFPATFVTAEMVPWEPGTWLISCOVNSHFRDGMOALYKVKSCSMAPPVDLL TGKVRQYFIEAHEIQWDYGPMGHDGSTGKNLREPGSISDKFFQKSSSRIGGTYWKVRYEAFQD ETFQEKMHLEEDRHLGILGPVIRAEVGDTIQVVFYNRASQPFSMQPHGVFYEKDYEGTVYNDG ${\tt SSYPGLVAKPFEKVTYRWTVPPHAGPTAQDPACLTWMYFSAADPIRDTNSGLVGPLLVCRAGA}$ LGADGKQKGVDKEFFLLFTVLDENKSWYSNANQAAAMLDFRLLSEDIEGFQDSNRMHAINGFL FSNLPRLDMCKGDTVAWHLLGLGTETDVHGVMFQGNTVQLQGMRKGAAMLFPHTFVMAIMQPD NLGTFEIYCQAGSHREAGMRAIYNVSQCPGHQATPRQRYQAARIYYIMAEEVEWDYCPDRSWE REWHNQSEKDSYGYIFLSNKDGLLGSRYKKAVFREYTDGTFRIPRPRTGPEEHLGILGPLIKG EVGDILTVVFKNNASRPYSVHAHGVLESTTVWPLAAEPGEVVTYOWNIPERSGPGPNDSACVS WIYYSAVDPIKDMYSGLVGPLAICQKGILEPHGGRSDMDREFALLFLIFDENKSWYLEENVAT HGSQDPGSINLQDETFLESNKMHAINGKLYANLRGLTMYOGERVAWYMLAMGQDVDLHTIHFH AESFLYRNGENYRADVVDLFPGTFEVVEMVASNPGTWLMHCHVTDHVHAGMETLFTVFSRTEH LSPLTVITKETEKVPPRDIEEGNVKMLGMOIPIKNVEMLASVLVAISVTLLLVVLALGGVVWY QHRQRKLRRNRRSILDDSFKLLSFKO

Signal peptide:

amino acids 1-21

Transmembrane domain:

amino acids 1109-1130

N-glycosylation sites.

amino acids 167-171, 239-243, 591-595, 717-721, 761-765, 832-836, 876-880, 934-938

Glycosaminoglycan attachment site.

amino acids 871-875

Tyrosine kinase phosphorylation sites.

amino acids 82-90, 137-145, 494-502, 513-521

N-myristoylation sites.

amino acids 212-218, 313-319, 498-504, 566-572, 672-678, 778-784, 843-849

Multicopper oxidases signature 1.

amino acids 344-365, 696-717, 1043-1064

Multicopper oxidases signature 2.

amino acids 1048-1060

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FIGURE 235

GGAAAGAGTGCTGGTACTACAACCAGGAAGTGACAGATAATGTGCTTTAAACTACATTAGAAAAGCTTCTCATAG CAAAACTGAGAGATTGAAGCAGTGATTATTTTTACATAGTTGTCATTAAATATTTTGGAGCTCTGCTGTGCATAGA GATGGCAACATACTTAGAATACACAGCTTTCTGGGCCAGAAATTGATCTTCTGACTTTTGAGCCTTATCTGATTA CTGCTTGGTTCATCTTTATTTTGTTAAACTACTCTGTAGGCTGAAAGGGAGAGACTCTCCTTGGTTTGCAGAGCC TGACTAGACAGGAATTCTGGCAACTGCTCCAGCAGAACTATGGCACTGAGCTAGGTTTAAATGCTGAGGAGATGG AAAACTTGTCACTGTCGATTGAGGATGTGCAGCCAAGAAGTCCAGGAAGAAGCAGCTTGGATGACTCTGGGGAGA GAGATGAAAAATTATCCAAGTCAATCAGTTTTACCAGTGAATCAATTAGTCGGGTTTCAGAAACAGAGTCATTCG ATGGAAATTCATCAAAAGGAGGATTAGGCAAAGAGGAGTCCCAAAATGAGAAACAGACCAAAAAAGAGTCTCTTAC CAACTTTGGAAAAGAAGTTAACTAGAGTGCCATCAAAGTCACTGGACTTGAATAAAAATGAATATCTTTCTCTGG ACAAAAGCAGCACTTCAGATTCTGTTGATGAAGAAAATGTTCCTGAGAAAGATCTTCATGGAAGACTTTTTATCA ACCGTATTTTTCATATCAGTGCTGACAGAATGTTTGAATTGCTCTTTACCAGTTCACGCTTTATGCAGAAATTTG CCAGTTCTAGAAATATAATAGATGTAGTATCTACCCCTTGGACTGCAGAACTTGGAGGTGATCAGCTGAGAACGA TGACCTACACTATAGTCCTTAATAGTCCACTTACTGGAAAATGCACTGCTGCCACTGAAAAGCAGACACTGTATA AAGAAAGTCGGGAAGCACGATTTTATTTGGTAGATTCAGAAGTACTGACACATGATGTCCCCTACCATGATTACT TCTATACCGTGAACAGATACTGTATCATCCGATCTTCAAAACAGAAATGCAGGCTAAGAGTTTCCACAGATTTGA AATACAGAAAACAGCCATGGGGCCTTGTCAAATCTTTAATTGAAAAGAATTCCTGGAGTTCTTTGGAGGACTATT TCAAACAGCTTGAATCAGATTTGTTAATTGAAGAATCTGTATTAAATCAGGCCATTGAAGACCCTGGAAAACTTA $\tt CTGGCCTACGAAGGAGAGGCGAACCTTCAACCGAACAGCAGAAACAGTTCCTAAACTTTCCTCTCAGCATTCCT$ TAGAACATGCTGCTCAGTCCTTTTACCGTCTCCGCCTCCAAGAAGAGAAATCTTTAAATTTAGCCTCTGATATGG TGTCAAGAGCAGAAACTATTCAGAAGAATAAAGATCAGGCCCATCGTTTAAAGGGAGTGCTCCGAGACTCCATAG TGATGCTTGAACAGCTGAAGAGCTCACTCATTATGCTTCAGAAAACGTTTGATCTACTAAATAAGAATAAGACTG ${\tt GCATGGCTGTTGAAAGC\underline{TAC}TGATCTGAAGGACTAAAACCGCAGAGATACTTGGAACTTAAAGAAAATACCTGGA}$ AGAAAACCAGACGAATGAAGGATTTTGGCATAGAACATTTCTATGTTTTTTCATTATTGAGATTTCTAATATGAA TATTTTTAAGCTGTGAATTTCTTCAGTGAACCATGAAATATATTATAGAACTGAATTTCTCTGATACAAAAAGAA AATGACACCCTGAATTGAGTGGTATGGTCTCATTTCTACAGTGAAGTCTGATGCTTTGTTAGCACAGAATCCG TACATGTCCAATAGGTCGCTTTTGTAACTGAGATAAGACCAAGAGGATAAACAGGACAATATAAGAAGAAACCTC TATGTCATTACTGATTTTAAAGGTTCTGTTTTCAGGCATATAACATTTCCAGGTTTGTGTACTGTAAAGATTATA ATGTCTTCATTTATTTAGCATGCAAATTTAATAGTCAAACTTTTTTGAATCTGCATGTTGATGATGATTATCAGAA AGGGTCTTCTGCCATGCTGTATCTTTATGAAAGAAATAGTTGTTTTTTCTTAAGGTAACTATCAGAGGTGGGATT ATCTTGCCTCCTCACTTAGAATACCAACAGTCAAAAGGAAGAACCATCCTCTGAGTTTTAAAAAACCAGAAGGTTA TGTTAAAATCTGGGCATTTAGTGACAGATCAAATGCATACTTGAACTAAGATTGGCTTCAGCTTAGCAGTCTTTC $\tt ATGGTGGAAGTGACACCTTGGTTGAAAATAATTTGTGTATTTTCAGTAACCATGTATGGCTTCCTTTTATGT$ ${\tt ATGTGTGTGACTTGTTTAATTGGTAAGTTATAAGCCAGACATAGATTTTAGCTCTTTAATAAAAACTTCAGGGG}$ CACGTATGTCCCAGTACAAGTGTACTGACTATCAAGTTTTAACTCAGATGCAAGCTTTGGCTCTTTCATAAAAAG TTTTTATGCATATGTGTCTCCATACAAGTGGCTCATTAAAATAAGAACTTTGTAAACTGACTTAAAATCAGATAT TTTTTCAAGAGTTAGGGAAAGTTGAAGTGTTTTACTGTTTTGTCTCTTGAGCCCTTTCTCTGGGGAAAAAAATACA TTTCATTTTTCTCCAGAGTCCCCAAAGCCACATGGCATTATTATAGTCATTTTTGAGATGCCTGTAGAGAATGAA AGTATTGACTCCGTTAGAGGGAAAATGGGTTTCTCTGGGTGAATTCCAACGAAGCATACCTAGGGGTAACAGTGA ACCTACCTGGGTTTGTTTTGTTTTGGTAAGGATTTATGTAGTGTCTGGCTGTAAGCAAGAATGAGTGGATTATAA ATTTTATAACATACTTCAAGGAAGAGTATCGAAGTAAGTTGCTTTATAAATTAAGACTAAATTCGTATGGATGCA GAATTCAATTAATAAAATTTGAGCCTGTTACGTAAATTGAATATTAATAAAATTGAAAATTTCAAAA

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FIGURE 236

MENLSLSIEDVQPRSPGRSSLDDSGERDEKLSKSISFTSESISRVSETESFDGNSSKGGLGKE
ESQNEKQTKKSLLPTLEKKLTRVPSKSLDLNKNEYLSLDKSSTSDSVDEENVPEKDLHGRLFI
NRIFHISADRMFELLFTSSRFMQKFASSRNIIDVVSTPWTAELGGDQLRTMTYTIVLNSPLTG
KCTAATEKQTLYKESREARFYLVDSEVLTHDVPYHDYFYTVNRYCIIRSSKQKCRLRVSTDLK
YRKQPWGLVKSLIEKNSWSSLEDYFKQLESDLLIEESVLNQAIEDPGKLTGLRRRRRTFNRTA
ETVPKLSSQHSSGDVGLGAKGDITGKKKEMENYNVTLIVVMSIFVLLLVLNVTLFLKLSKIE
HAAQSFYRLRLQEEKSLNLASDMVSRAETIQKNKDQAHRLKGVLRDSIVMLEQLKSSLIMLQK
TFDLLNKNKTGMAVES

Transmembrane domain:

amino acids 352-371

N-glycosylation sites.

amino acids 3-7, 54-58, 312-316, 349-353, 367-371, 449-453

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 81-85, 307-311

Tyrosine kinase phosphorylation sites.

amino acids 202-211, 246-254, 341-349

N-myristoylation site.

amino acids 259-265

Amidation site.

amino acids 339-343

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FIGURE 237

CAGGGGCTGGAGGGCAGGGGAGGGATCATGTCATTCCTGCTCGGCGCAATCCTGACCCTGCT
CTGGGCGCCCACGGCTCAGGCTGAGGTTCTGCTGCAGCCTGACTTCAATGCTGAAAAGTTCTC
AGGCCTCTGGTACGTGGTCTCCATGGCATCTGACTGCAGGGTCTTCCTGGGCAAGAAGGACCA
CCTGTCCATGTCCACCAGGGCCATCAGGCCCACAGAGGAGGGCGGCCTCCACGTCCACATGGA
GTTCCCGGGGGCCGACGGCTGTAACCAGGTGGATGCCGAGTACCTGAAGGTGGGCTCCGAGGG
ACACTTCAGAGTCCCGGCCTTGGGCTACCTGGACGTGCGCATCGTGGACACAGACTACAGGTC
CTTCGCCGTCCTTTACATCTACAAGGAGCTGGAGGGGCCCTCAGCACCATGGTGCAGCTCTA
CAGCCGGACCCAGGATGTGAGTCCCCAGGCTCTGAAGTCCTTCCAGGACTTCTACCCGACCCT
GGGGCTCCCCAAGGACATGATGGTCATGCTGCCCCAGTCAGATGCAACCCTGAGAGCAA
GGAGGCGCCCTGACACCTCCGGAGCCCCACCCCCGCCCTTCCCAGGTGGAGCCAAAGCAGCAG
GCGCCTTTGCCCCTGGAGTCAAGACCCACAGCCCTCGGGGACCACCTGGAGTCTCCCATCCT
CCACCCCCCGCCTGTGGGATGCCTTGTGGGGACGTCTCTTTCTATTCAATAAACAGATGCTGCA
GCCTCA

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FIGURE 238

MMSFLLGAILTLLWAPTAQAEVLLQPDFNAEKFSGLWYVVSMASDCRVFLGKKDHLSMSTRAI RPTEEGGLHVHMEFPGADGCNQVDAEYLKVGSEGHFRVPALGYLDVRIVDTDYSSFAVLYIYK ELEGALSTMVQLYSRTQDVSPQALKSFQDFYPTLGLPKDMMVMLPQSDACNPESKEAP

Signal peptide:

amino acids 1-20

Tyrosine kinase phosphorylation site.

amino acids 110-117

N-myristoylation sites.

amino acids 7-13, 79-85, 130-136

Amidation site.

amino acids 50-54

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FIGURE 239

GCCAAGTCCGGGGCCCGCCGCTGCCTAGCGCGTCCTGGGGACTCTGTGGGGACGCGCCCCG CGCCGCGCTCGGGGACCCGTAGAGCCCGGCGCTGCGCGCATGGCCCTGCTCTCGCGCCCCGC GCTCACCCTCCTCCTCCTCATGGCCGCTGTTGTCAGGTGCCAGGAGCAGGCCCAGACCAC CGACTGGAGAGCCACCCTGAAGACCATCCGGAACGGCGTTCATAAGATAGACACGTACCTGAA CGCCGCCTTGGACCTCCTGGGAGGCGAGGACGGTCTCTGCCAGTATAAATGCAGTGACGGATC TAAGCCTTTCCCACGTTATGGTTATAAACCCTCCCCACCGAATGGATGTGGCTCTCCACTGTT CTATGAGACCTGTGGCAAAAGCAAGAATGACTGTGATGAAGAATTCCAGTATTGCCTCTCCAA GATCTGCCGAGATGTACAGAAAACACTAGGACTAACTCAGCATGTTCAGGCATGTGAAACAAC AGTGGAGCTCTTGTTTGACAGTGTTATACATTTAGGTTGTAAACCATATCTGGACAGCCAACG AGCCGCATGCAGGTGTCATTATGAAGAAAAACTGATCTT**TAA**AGGAGATGCCGACAGCTAGT GACAGATGAAGATGGAAGAACATAACCTTTGACAAATAACTAATGTTTTTACAACATAAAACT GTCTTATTTTTGTGAAAGGATTATTTTGAGACCTTAAAATAATTTATATCTTGATGTTAAAAAC CTCAAAGCAAAAAAGTGAGGGAGATAGTGAGGGGAGGGCACGCTTGTCTCTCAGGTATCTT CCCCAGCATTGCTCCCTTACTTAGTATGCCAAATGTCTTGACCAATATCAAAAACAAGTGCTT GTTTAGCGGAGAATTTTGAAAAGAGGAATATATAACTCAATTTTCACAACCACATTTACCAAA AAAAGAGATCAAATATAAAATTCATCATAATGTCTGTTCAACATTATCTTATTTGGAAAATGG GGAAATTATCACTTACAAGTATTTGTTTACTATGAAATTTTAAATACACATTTATGCCTAGAA GGAACGGACTTTTTTTTTTTTTTATTTAATTACACATAATATGTAATTAAAGTACAACATAATAT GTTGTTTCTCTGTAGCCCGTTGAGCATATGAGTAAGTCACATTTCTATTAGGACTACTTACAA GGACAAGGTTTCCATTTTTCCAGTTGTAAAATTGGAACCATCAGCTGATAACCTCGTAGGGAG CAACCCCAGGATAGCTAAGTGTTATGTAATATGCCTAGAAGGTGATGTGAATGCGATTCAGAA GCATAGCCACTCCCATTTTATGAGCTACTCACATGACAAATGTCATCTTTTGCTATAACCTTT AAAAAAAAAAAAAA

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FIGURE 240

MALLSRPALTLLLLLMAAVVRCQEQAQTTDWRATLKTIRNGVHKIDTYLNAALDLLGGEDGLC QYKCSDGSKPFPRYGYKPSPPNGCGSPLFGVHLNIGIPSLTKCCNQHDRCYETCGKSKNDCDE EFQYCLSKICRDVQKTLGLTQHVQACETTVELLFDSVIHLGCKPYLDSQRAACRCHYEEKTDL

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites:

amino acids 57-63,93-99

Phospholipase A2 histidine active site:

amino acids 106-114

Neuraxin and MAP1B proteins repeat proteins Block:

amino acids 109-137

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FIGURE 241

CCCTGAGAGTCTGAGCGCTCGCCGCACCCCCTTCCGAGCTTCTATTGGCCGTAGCAGACGTCC GTCTGCCGCTATCTCCGCCCCAATACGGAAGCGGCCTAGTCCTCCGGCTCCGACAGCTGGGTG TCGTGCTCACCGCGCTGTGGGCCGCGCCGTGGGCCTGGAGCTGCCTTACGTGCTGCTCC GTCCCGGGCCGCCGCTGGGACCCCTGGCCCGGGCCTTGCAGCTGGCGCTGGCCGCCTTCC AGCTGCTCAACCTGCTGGGCAACGTGGGGCTCTTCCTGCGCTCGGATCCCAGCATCCGTGGCG TGATGCTGGCCGGCCGCGTCTGGGCCAGGGCTGGGCTTACTGCTACCAATGCCAAAGCCAGG TGCCGCCACGCAGCGGACACTGCTCTGCCTGCCGCGTCTGCATCCTGCGTCGGGACCACCACT GCCGCCTGCTGGGCCGCTGCGTGGGCTTCGGCAACTACCGGCCCTTCCTGTGCCTGCTTC ATGCCGCCGGCGTCCTCCACGTCTCTGTGCTGCTGGGCCCTGCACTGTCGGCCCTGCTGC GAGCCCACACGCCCTCCACATGGCTGCCTCCTCCTGCTTCCCTGGCTCATGTTGCTCACAG TGCTGTGCGGGGCTGCTCTTCCATGGGATGCTGCTGCTGCGGGGCCAGACCACATGGG GGCCCGCTGGGCCTCGTCTGGCCTCTGGCCCTTCCTGGCCTCCCCATTGCCTGGGGATGGGA TCACCTTCCAGACCACAGCAGATGTGGGACACACAGCCTCC**TGA**CTCCAGGAAGAGCCAGAGC TGTGCAGGGAGGAGGGGTGAGAGGGGGGCCCCCACACCTAGACTCAGTAAGGAAGTCGGGTT CTCCTACGTGTCCAGGGCTTGGGCCGTGACTTAGGCAGAGGAGTGCAGAGGAGGGTCTGGCAG GGGCTGCTCAGGCCGCCTAGCTGCCCCTTTGCCAGGTTAATAAAGCACTGACTTGTTAA

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FIGURE 242

MGQPWAAGSTDGAPAQLPLVLTALWAAAVGLELAYVLVLGPGPPPLGPLARALQLALAAFQLL
NLLGNVGLFLRSDPSIRGVMLAGRGLGQGWAYCYQCQSQVPPRSGHCSACRVCILRRDHHCRL
LGRCVGFGNYRPFLCLLLHAAGVLLHVSVLLGPALSALLRAHTPLHMAALLLLPWLMLLTGRV
SLAQFALAFVTDTCVAGALLCGAGLLFHGMLLLRGQTTWEWARGQHSYDLGPCHNLQAALGPR
WALVWLWPFLASPLPGDGITFQTTADVGHTAS

Important features:

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 51-66,143-160,174-191,198-214

N-myristoylation sites:

amino acids 2-8,8-14,30-36,81-87,88-94,90-96,206-212

Leucine zipper pattern:

amino acids 143-165,150-172,157-179,164-186

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FIGURE 243

CTTGTCTTTGTGTCGGTTGTGATTTTCCTAATCTCTGATTTTCCTTTTCTCTCGGACGCTCTC CCTCTTCGGACCCATTTTCTCCCGTGCTTCATGCCCTGATAGCCTGGCCCCTTCCCGGCTTCC CTTCCTCAAGAGTTCGCCCCTCTGGGGGCTCCTCTGTGTAATCGTCGCCTTCTCTGGGTATTT CTGTGAACTCCGTCTCACACCATCCCGCCATCTTCTCTGCCTTGGCCCCTTTTCTCTGTACAG CCAGCTCTGTGTCCTTTTCTTCTCCCCCTCTAAAATCGACTCCTCTTCTCCCTGAGAGCCCCA CAAGGTTCCATTCCATCAATTTGTTTTGTCTTTTGTAGGGGTTGGCATCCCCTCTGACTACTGCT CCATCCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGCTTGAGGATTTCACTTCAATCTTTTCTGGT TGCGTCTCCACTTGTACTCAGCTTGTTAGGTCCAGGTCCAGTTGTTCTGCATCTGAGGCTGGC GTGTGCTGTCTTCTCTGATTGGCCTAATCTCCCTCACCCCGTGAGATCTGTTGTCAGCCTTC GTTTCTCTTTCCTGTGTCCCAGCTTTTCTGCGGGTCTTGGCACCTTTCTTGGCCACAGATTTC TGGGTTACAGAGCATGTGTGTCTGAGGCATTGCAGGCAGAAAAGGGTGGCCGACGTGACCTCT CAGGTGGACAAAGAATTCGGGGACTGATGGGAACTGAGCTTGGGATCCAGACTGAAACTGATT CCAGACTGACCTCTAGCACCCAGGACCCAGACACAGGGCCATGGGACCCCAGCATTTGAGACT TGTGCAGCTGTTCTGCCTTCTAGGGGCCATCCCCACTCTGCCTCGGGCTGGAGCTCTTTTGTG CTATGAAGCAACAGCCTCAAGATTCAGAGCTGTTGCTTTCCATAACTGGAAGTGGCTTCTGAT GAGGAACATGGTGTAAGCTGCAAGAGGGCTGCGAGGAGACGCTAGTGTTCATTGAGACAGG GACTGCAAGGGGAGTTGTGGGCTTTAAAGGCTGCAGCTCGTCTTCGTCTTACCCTGCGCAAAT CTCCTACCTTGTTTCCCCACCCGGAGTGTCCATTGCCTCCTACAGTCGCGTCTGCCGGTCTTA TCTCTGCAACAACCTCACCAATTTGGAGCCTTTTGTGAAACTCAAGGCCAGCACTCCTAAGTC TATCACATCTGCGTCCTGTAGCTGCCCGACCTGTGTGGGCCGAGCACATGAAGGATTGCCTCCC AAATTTTGTCACCACTAATTCTTGCCCCTTGGCTGCTTCTACGTGTTACAGTTCCACCTTAAA ATTTCAGGCAGGGTTTCTCAATACCACCTTCCTCCTCATGGGGTGTGCTCGTGAACATAACCA GCTTTTAGCAGATTTTCATCATATTGGGAGCATCAAAGTGACTGAGGTCCTCAACATCTTAGA GAAGTCTCAGATTGTTGGTGCAGCATCCTCCAGGCAAGATCCTGCTTGGGGTGTCGTCTTAGG $\verb|CCTCCTGTTTGCCTTCAGGGAC| \textbf{TGA}| CCATCTAGCTGCACCCGACAAGCACCCAGACTCTTTCA|$ AAAAAAAA

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FIGURE 244

MGPQHLRLVQLFCLLGAIPTLPRAGALLCYEATASRFRAVAFHNWKWLLMRNMVCKLQEGCEE TLVFIETGTARGVVGFKGCSSSSSYPAQISYLVSPPGVSIASYSRVCRSYLCNNLTNLEPFVK LKASTPKSITSASCSCPTCVGEHMKDCLPNFVTTNSCPLAASTCYSSTLKFQAGFLNTTFLLM GCAREHNQLLADFHHIGSIKVTEVLNILEKSQIVGAASSRQDPAWGVVLGLLFAFRD

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation sites:

amino acids 117-121, 183-187

N-myristoylation sites:

amino acids 16-22,25-31,60-66,71-77,81-87,100-106,224-230, 235-241,239-245

Prokaryotic membrane lipoprotein lipid attachment site:

amino acids 181-192

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FIGURE 245

GTGGAGTTGGGTGTCGGGAGCCTCTCCCTGAGGGGCACCGCGTCTTCAGGAGCTGGGCCTCCAGTGCGGCGC GATGTCAGGCGCGGTGACAGCTCTGTGAGTCCGAGGCCGCGGCCGTGGCGCTGGGCGGCTGCGGGGCCTGACCGG TCCGCTC<u>ATG</u>GTGCCGCCACGACGCCATCGCGGGGCAGGAAGGCCAGGGGTGCTGAGTTCTTCACCTCCTTTTAG ACTGAGATCTGCCAAGTTTTCCGGCATTGCTCTTGAGGATCTCAGAAGGGCTCTTAAGACAAGACTGCAAATGGT GTGTGTATTTGTCATGAACCGAATGAATTCCCAGAACAGTGGTTTCACTCAGCGCAGGCGAATGGCTCTTGGGAT CAAACCATTCTTCAGCACCTTTGCAAAAACATCTATGTTTTGTTTTTGTACCTTTTTGGGCTTTATTATTTTGGAAGCC TGCTTGCACAACAGATACAACTATGAATAGTTCTTTGAGTGAACCTCTGTATGTGCCTGTGAAATTCCATGATCT TCCAAGTGAAAAACCTGAGAGCACAAACATTGATACTGAAAAAAACCCCCAAAAAGTCTCGTGTGAGGTTCAGTAA TATCATGGAGATTCGACAGCTTCCGTCAAGTCATGCATTGGAAGCAAAGTTGTCTCGCATGTCATATCCTGTGAA CTTTGTGTGTGTTTTTGGCAAATTTGTCATATCAAGAAGCACTTTCAGACACACAAGTTGCTATAGTTAATATTTT TTCTAAACTATTAGCTGTAATTTTAAGCATTGGAGGCGTTGTACTGGTAAACCTGGCAGGGTCTGAAAAACCTGC TGGAAGACACAGTAGGTTCCATTTGGTCTCTTGCTGGAGCCATGCTCTATGCTGTCTATATTGTTATGATTAA GAGAAAAGTAGATAGAGAAGACAAGTTGGATATTCCAATGTTCTTTGGTTTTGTAGGTTTTGTTAATCTGCTGCT CTTATGGCCAGGTTTCTTTTTACTTCATTATACTGGATTTGAGGACTTCGAGTTTCCCAATAAAGTAGTATTAAT GTGCATTATCATTAATGGCCTTATTGGAACAGTACTCTCAGAGTTCCTGTGGTTGTGGGGCTGCTTTCTTACCTC ATCATTGATAGGCACACTTGCACTAAGCCTTACAATACCTCTGTCCATAATAGCTGACATGTGTATGCAAAAGGT TTATAATAATTGGGATCCTGTGATGGTGGGAATCAGAAGAATATTTGCTTTTATATGCAGAAAACATCGAATTCA GAGAGTTCCAGAAGACAGCGAACAGTGTGAGAGTCTCATTTCTATGCACAGTGTTTCTCAGGAGGATGGAGCTAG TTAGCTGTCTGTTGTCTGTAGCCCAGCTTGATAATGGAACTATACAGCGAAGAGACAATCTCTGGCAAGTTTTTG TAGAAAAATGTTTCAGTGCCTAGTCTGAAAAATAACAGTTTTGAGTTCTTTGAAACTCTAAAATATATTTTTCTC ATACCTGTTTTCTTCATTTCATAATGAAGCACTTTGCTATGTAGCTGTGTACATATCACTACAGTTATAGGAAG TTTCAGTCTACAGTCCAAAGGACCAACCTGCCTTACACATCTCAAGGAATTCAGCTGTTGAAATCATTTGA ACTAATCAAGGAATAAATCCTAATGTTCTGGGACTTTATTTTCACATGTTAAATGCTGGAATATATTATGAAAAT GTTTTCAAGAAATCACTTAAGTGTTCATAGACCAGTATTTCTGACAGGTAAAATGCTAAAATAAGCTACCTGTAA TAAGTGTGGATTATATTTTTGGGTTTTGTAGAATATTGCAAATTAACCACAAAAAAATGTTTAATTTATGCAAC AAGCATGTTTGTGCAAATTTCATGGGACTTTAAAAAGAATAAGTATTTGAGAAAATATCTGGTTCACTTACACTA CATTTACTGTATTATTCTTTTATAGCATTAGGTGCCTTGTATTTTAAATCTGTGACAAACCATGGCAAATTTTTA AAGGGGAAGTATTATTATAAAATGAAGAAATATGTATTTCTAAAGGCTATATTGCTGTAAACTTAATTGATAAAG CTCTGTTTAATTTAGAGTTTTGAAGAAATAGTCTCCCTTCAATTAAGAAATTTTCATAATGGAATGATTTAAATT GAAGTGACAAAGAGTATTATTAAAATACAATGTTTATAAAAAAA

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FIGURE 246

MVPPRRHRGAGRPGVLSSSPPFRLRSAKFSGIALEDLRRALKTRLQMVCVFVMNRMNSQNSGF
TQRRRMALGIVILLLVDVIWVASSELTSYVFTQYNKPFFSTFAKTSMFVLYLLGFIIWKPWRQ
QCTRGLRGKHAAFFADAEGYFAACTTDTTMNSSLSEPLYVPVKFHDLPSEKPESTNIDTEKTP
KKSRVRFSNIMEIRQLPSSHALEAKLSRMSYPVKEQESILKTVGKLTATQVAKISFFFCFVWF
LANLSYQEALSDTQVAIVNILSSTSGLFTLILAAVFPSNSGDRFTLSKLLAVILSIGGVVLVN
LAGSEKPAGRDTVGSIWSLAGAMLYAVYIVMIKRKVDREDKLDIPMFFGFVGLFNLLLLWPGF
FLLHYTGFEDFEFPNKVVLMCIIINGLIGTVLSEFLWLWGCFLTSSLIGTLALSLTIPLSIIA
DMCMQKVQFSWLFFAGAIPVFFSFFIVTLLCHYNNWDPVMVGIRRIFAFICRKHRIQRVPEDS
EQCESLISMHSVSQEDGAS

Important features:

Transmembrane domain:

amino acids 69-87,105-118,237-256,266-285,300-316,332-346, 364-379,399-419,453-472

N-glycosylation sites:

amino acids 157-161,255-259

N-myristoylation sites:

amino acids 14-20,329-335,404-410,407-413,418-424

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FIGURE 247

CGTCTGTAGAGATATCATGAACTTCAACTTAGCTTTGGTACTTTCTTCCCTGAAGACAGAGGG CAGAACTCTGAGTTCCAGAACCATTTTCAACTGTATTGGGGACCAATCACTTGACTCTATTCT TGTCTCTGACAGATGACGCTACACTCTCCTCTGAATAATGGACACCATTTCTAAAACTGAA TCCTGCTACTAAAATAATTCAGATGATATTTTTTCCAATTCTACAATCTTGCTTTGTTTTAT TTAGTTGTTTTCTCTCTCTCTCTCCCAGTTTTCCAGAGACTGGAGCTAAACTGGGCTTTCAACA TCATCATGAAGTTTATCCTCCTCTGGGCCCTCTTGAATCTGACTGTTGCTTTGGCCTTTAATC CAGATTACACAGTCAGCTCCACTCCCCCTTACTTGGTCTATTTGAAATCTGACTACTTGCCCT GCGCTGGAGTCCTGATCCACCCGCTTTGGGTGATCACAGCTGCACACTGCAATTTACCAAAGC TTCGGGTGATATTGGGGGTTACAATCCCAGCAGACTCTAATGAAAAGCATCTGCAAGTGATTG GCTATGAGAAGATGATCATCATCACACTTCTCAGTCACTTCTATTGATCATGACATCATGC TAATCAAGCTGAAAACAGAGGCTGAACTCAATGACTATGTGAAATTAGCCAACCTGCCCTACC ACAAAGAGCCCGATTCACTGCAAACTGTGAACATCTCTGTAATCTCCAAGCCTCAGTGTCGCG GGCAGCCCTGCAAGGAAGTTTCTGCTGCCCCGGCAATCTGCAATGGGATGCTTCAAGGAATCC TGTCTTTTGCGGATGGTTTTTGAGAGCCGATGTTGGCATCTATGCCAAAATTTTTTACT ATATACCCTGGATTGAAAATGTAATCCAAAATAAC**TGA**GCTGTGGCAGTTGTGGACCATATGA

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FIGURE 248

MKFILLWALLNLTVALAFNPDYTVSSTPPYLVYLKSDYLPCAGVLIHPLWVITAAHCNLPKLR VILGVTIPADSNEKHLQVIGYEKMIHHPHFSVTSIDHDIMLIKLKTEAELNDYVKLANLPYQT ISENTMCSVSTWSYNVCDIYKEPDSLQTVNISVISKPQCRDAYKTYNITENMLCVGIVPGRRQ PCKEVSAAPAICNGMLQGILSFADGCVLRADVGIYAKIFYYIPWIENVIQNN

Important features:

Signal peptide:

amino acids 1-17

N-glycosylation sites:

amino acids 11-15,156-160,173-177

Tyrosine kinase phosphorylation site:

amino acids 108-117

N-myristoylation sites: amino acids 182-188,203-209

Amidation site:

amino acids 185-189

Serine proteases, trypsin family, histidine active site:

amino acids 52-58

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FIGURE 249

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FIGURE 250

MWWLSIGALIGLSVAAVVLLAFIVTACVLCYLFISSKPHTKLDLGLSLQTAGPEEVSPDCQGV NTGMAAEVPKVSPLQQSYSCLNPQLESNEGQAVNSKRLLHHCFMATVTTSDIPGSPEEASVPN PDLCGPVP

Important features:

Signal peptide:

Amino acids 1-26

N-myristoylation sites:

Amino acids 7-13,11-17,62-68,93-99

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FIGURE 251

GTGGTTTGGATTGAGCCGGGCCGGCCGGGCCGGGCCGAGTCGGAGGGGGTGGCAGTGAGCGGCG GCAGAGGCTACGGGGCTCGGTTTGGCTGACTGGGGAGTCGGCAGGCGGCAGGAACC<u>ATG</u>CGAG ACAGGCGCCGCTGTCCACCTCTACTCCGGGGTCTAGTACAGCGCTGGCGCTACGGCAAGGTCT GCCTGCGCTCCTGCTCTACAACTCCTTTGGGGGCAGTGACACCGCTGTTGATGCTGCCTTTG AGCCTGTCTACTGGCTGGTAGACAACGTGATCCGCTGGTTTTGGAGTGGTGTTCGTGGTCCTGG TGATCGTGCTGACAGGCTCCATTGTAGCTATCGCCTACCTGTGTGTCCTGCCTCTCATCCTCC GAACCTACTCAGTGCCACGACTCTGCTGGCATTTCTTCTATAGCCACTGGAATCTGATCCTGA GCAGCATCTGCAACAGGTGTGTGCTGAAGATGGATCACCACTGCCCCTGGCTAAACAATTGTG TGGGCCACTATAACCATCGGTACTTCTTCTTTTCTGCTTTTTCATGACTCTGGGCTGTGTCT ACTGCAGCTATGGAAGTTGGGACCTTTTCCGGGAGGCTTATGCTGCCATTGAGACTTATCACC AGACCCCACCACCTTCTCCTTTCGAGAAAGGATGACTCACAAGAGTCTTGTCTACCTCT GGTTCCTGTGCAGTTCTGTGGCACTTGCCCTGGGTGCCCTAACTGTATGGCATGCTGTTCTCA TCAGTCGAGGTGAGACTAGCATCGAAAGGCACATCAACAAGAAGGAGACGTCGGCTACAGG CCAAGGGCAGAGTATTTAGGAATCCTTACAACTACGGCTGCTTGGACAACTGGAAGGTATTCC TGGGTGTGGATACAGGAAGGCACTGGCTTACTCGGGTGCTCTTACCTTCTAGTCACTTGCCCC CAGTGTGAGCTGGACTGTGTCAGCCACGACTCGAGCACTCATTCTGCTCCCTATGTTATTTCA GGAGAAATCTTAGGACTGACATCCCTTTACTCAGGCAAACAGAAGTTCCAACCCCAGACTAGG GGTCAGGCAGCTAGCTACCTTGCCCAGTGCTGACCCGGACCTCCTCCAGGATACAGCAC TGGAGTTGGCCACCACCTCTTCTACTTGCTGTCTGAAAAAAACACCTGACTAGTACAGCTGAGA TCTTGGCTTCTCAACAGGGCAAAGATACCAGGCCTGCTGAGGTCACTGCCACTTCTCACA AAAAAAAAAA

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FIGURE 252

MRGQRSLLLGPARLCLRLLLLLGYRRRCPPLLRGLVQRWRYGKVCLRSLLYNSFGGSDTAVDA
AFEPVYWLVDNVIRWFGVVFVVLVIVLTGSIVAIAYLCVLPLILRTYSVPRLCWHFFYSHWNL
ILIVFHYYQAITTPPGYPPQGRNDIATVSICKKCIYPKPARTHHCSICNRCVLKMDHHCPWLN
NCVGHYNHRYFFSFCFFMTLGCVYCSYGSWDLFREAYAAIETYHQTPPPTFSFRERMTHKSLV
YLWFLCSSVALALGALTVWHAVLISRGETSIERHINKKERRRLQAKGRVFRNPYNYGCLDNWK
VFLGVDTGRHWLTRVLLPSSHLPHGNGMSWEPPPWVTAHSASVMAV

Important features:

Transmembrane domain:

amino acids 88-100,202-216,254-274

N-myristoylation sites:

amino acids 55-61,56-62,92-98,210-216,309-315,319-325,340-346

Prokaryotic membrane lipoprotein lipid attachment site:

amino acids 201-212

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FIGURE 253

GATCAAGCGCCTTCCTTTCCCTTCTCCCTACTTGGCCTTTGCCCTAAGCCAAGACCTGGCCATCAGCCTGGC ${\tt TGCAGGGGCCTGCAGAGCCAGCTGCACTTTTTCAGGTATGGGGGAGGGCCAGGCACC} {\tt ATG} {\tt AAGCCAGTGTGGGTC}$ GCCACCCTTCTGTGGATGCTACTGCTGGTGCCCAGGCTGGGGGCCCCCGGAAGGGGTCCCCAGAAGAGGCCTCC TTCTACTATGGAACCTTCCCTCTTGGCTTCTCCTGGGGCGTGGGCAGTTCTGCCTACCAGACGGAGGGCGCCTGG ACGGCAGATGTAGCCTGTGACGGCTACTACAAGGTCCAGGAGGACATCATTCTGCTGAGGGAACTGCACGTCAAC CACTACCGATTCTCCCTGTCTTGGCCCCGGCTCCTGCCCACAGGCATCCGAGCCGAGCAGGTGAACAAGAAGGGA ATCGAATTCTACAGTGATCTTATCGATGCCCTTCTGAGCAGCAACATCACTCCCATCGTGACCTTGCACCACTGG GCCAACCTGTGCTTTGAGGCCTTTGGGGACCGTGTGAAGCACTGGATCACGTTCAGTGATCCTCGGGCAATGGCA GAAAAAGGCTATGAGACGGCCACCATGCGCCGGGCCTGAAGCTCCGCGGCACCGGCCTGTACAAGGCAGCACAC GGAATTTCACTGAACTGTGACTGGGGGGAACCTGTGGACATTAGTAACCCCAAGGACCTAGAGGCTGCCGAGAGA TACCTACAGTTCTGTCTGGGCTGGTTTGCCAACCCCATTTATGCCGGTGACTACCCCCAAGTCATGAAGGACTAC ATTGGAAGAAGAGTGCAGAGCAAGGCCTGGAGATGTCGAGGTTACCGGTGTTCTCACTCCAGGAGAAGAGCTAC ATTAAAGGCACATCCGATTTCTTGGGATTAGGTCATTTTACTACTCGGTACATCACGGAAAGGAACTACCCCTCC CGCCAGGGGCCCAGCTACCAGAACGATCGTGACTTGATAGAGCTGGTTGACCCAAACTGGCCAGATCTGGGGTCT ATATATGTGATGGAAAATGGAGCATCTCAAAAATTCCACTGTACTCAATTATGTGATGAGTGGAGAATTCAATAC CTTAAAGGATACATAAATGAAATGCTAAAAGCTATAAAAGATGGTGCTAATATAAAGGGGTATACTTCCTGGTCT AATAAGCCTCGCTATCCAAAGGCTTCAGTTCAATATTACAAGAAGATTATCATTGCCAATGGGTTTCCCAATCCA TTGCTAAGTCACATGCAAATGGTTACGGAGATCGTGGTACCCACTGTCTGCTCCCTCTGTGTCCTCATCACTGCT GTTCTACTAATGCTCCTCCTGAGGAGGCAGAGCTGAGACAGGATTATCAATTTTGGAGCTTCATAAGAGAATCTT CAGGATCTTCCTCCCTTTTCTGCTTTGAGGGTTTCCATACATTGCTGTTTTCAGGTTCTACAATAATTACCTTTT TTTCTCTTTTTTGGCTTGTGCTGGGATTTAAGAATTAGAAAATAAAAATAAGCAGAAATTA

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FIGURE 254

MKPVWVATLLWMLLLVPRLGAARKGSPEEASFYYGTFPLGFSWGVGSSAYQTEGAWDQDGKGPSIWDVFTHSGKG
KVLGNETADVACDGYYKVQEDIILLRELHVNHYRFSLSWPRLLPTGIRAEQVNKKGIEFYSDLIDALLSSNITPI
VTLHHWDLPQLLQVKYGGWQNVSMANYFRDYANLCFEAFGDRVKHWITFSDPRAMAEKGYETGHHAPGLKLRGTG
LYKAAHHIIKAHAKTWHSYNTTWRSKQQGLVGISLNCDWGEPVDISNPKDLEAAERYLQFCLGWFANPIYAGDYP
QVMKDYIGRKSAEQGLEMSRLPVFSLQEKSYIKGTSDFLGLGHFTTRYITERNYPSRQGPSYQNDRDLIELVDPN
WPDLGSKWLYSVPWGFRRLLNFAQTQYGDPPIYVMENGASQKFHCTQLCDEWRIQYLKGYINEMLKAIKDGANIK
GYTSWSLLDKFEWEKGYSDRYGFYYVEFNDRNKPRYPKASVQYYKKIIIANGFPNPREVESWYLKALETCSINNQ
MLAAEPLLSHMQMVTEIVVPTVCSLCVLITAVLLMLLRRQS

Important features:

Signal peptide:

amino acids 1-21

Transmembrane domain:

amino acids 541-558

N-glycosylation sites:

amino acids 80-84,171-175,245-249

Glycosaminoglycan attachment site:

amino acids 72-76

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

amino acids 23-27,564-568

Tyrosine kinase phosphorylation sites:

amino acids 203-211,347-355,460-468,507-514

N-myristoylation sites:

amino acids 44-50,79-85,167-173,225-231,257-263,315-321

Amidation site:

amino acids 307-311

Glycosyl hydrolases family 1 active site:

amino acids 407-416

Glycosyl hydrolases family 1 N-terminal signature:

amino acids 41-56

Motif name Glycosyl hydrolases family:

amino acids 37-67

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FIGURE 255

CGCGAAG**ATG**CGAAAGGTGGTTTTGATCACCGGGGCTAGCAGTGGCATTGGCCTGGCCCTCTG CAAGCGGCTGCTGGCGGAAGATGATGAGCTTCATCTGTGTTTGGCGTGCAGGAACATGAGCAA GGCAGAAGCTGTCTGTGCTGCTGCTGGCCTCTCACCCCACTGCTGAGGTCACCATTGTCCA GGTGGATGTCAGCAACCTGCAGTCGGTCTTCCGGGCCTCCAAGGAACTTAAGCAAAGGTTTCA GAGATTAGACTGTATATATCTAAATGCTGGGATCATGCCTAATCCACAACTAAATATCAAAGC ACTTTTCTTTGGCCTCTTTTCAAGAAAAGTGATTCATATGTTCTCCACAGCTGAAGGCCTGCT GACCCAGGGTGATAAGATCACTGCTGATGGACTTCAGGAGGTGTTTGAGACCAATGTCTTTGG CCATTTTATCCTGATTCGGGAACTGGAGCCTCTCCTCTGTCACAGTGACAATCCATCTCAGCT CATCTGGACATCATCTCGCAGTGCAAGGAAATCTAATTTCAGCCTCGAGGACTTCCAGCACAG CAAAGGCAAGGAACCCTACAGCTCTTCCAAATATGCCACTGACCTTTTGAGTGTGGCTTTGAA CAGGAACTTCAACCAGCAGGGTCTCTATTCCAATGTGGCCTGTCCAGGTACAGCATTGACCAA TTTGACATATGGAATTCTGCCTCCGTTTATATGGACGCTGTTGATGCCGGCAATATTGCTACT TCGCTTTTTTGCAAATGCATTCACTTTGACACCATATAATGGAACAGAAGCTCTGGTATGGCT TTTCCACCAAAAGCCTGAATCTCTCAATCCTCTGATCAAATATCTGAGTGCCACCACTGGCTT TGGAAGAAATTATATTATGACCCAGAAGATGGACCTAGATGAAGACACTGCTGAAAAATTTTA TCAAAAGTTACTGGAACTGGAAAAGCACATTAGGGTCACTATTCAAAAAACAGATAATCAGGC CAGGCTCAGTGGCTCATGCCTA**TAA**TTCCAGCACTTTGGGAGGCCAAGGCAGAAGGATCACTT GAGACCAGGAGTTCAAGACCAGCCTGAGAAACATAGTGAGCCCTTGTCTCTACAAAAAGAAAT AAAAATAATAGCTGGGTGTGGTGGCATGCGCATGTAGTCCCAGCTACTCAGAAGGATGAGGTG GGAGGATCTCTTGAGGCTGGGAGGCAGAGGTTGCAGTGAGCTGAGATTGTGCCACTGCACTCC GAGCTGACAATGACACTCTGGAACATTGCATACCTTCTGTACATTCTGGGGTACATGGATTTC TACTGAGTTGGATAATATGCATTTGTAATAAACTATGAACTATGAA

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FIGURE 256

MRKVVLITGASSGIGLALCKRLLAEDDELHLCLACRNMSKAEAVCAALLASHPTAEVTIVQVD VSNLQSVFRASKELKQRFQRLDCIYLNAGIMPNPQLNIKALFFGLFSRKVIHMFSTAEGLLTQ GDKITADGLQEVFETNVFGHFILIRELEPLLCHSDNPSQLIWTSSRSARKSNFSLEDFQHSKG KEPYSSSKYATDLLSVALNRNFNQQGLYSNVACPGTALTNLTYGILPPFIWTLLMPAILLLRF FANAFTLTPYNGTEALVWLFHQKPESLNPLIKYLSATTGFGRNYIMTQKMDLDEDTAEKFYQK LLELEKHIRVTIQKTDNQARLSGSCL

Important features:

Transmembrane domain:

amino acids 234-254

N-glycosylation sites:

amino acids 37-41,178-182,229-233,263-267

Glycosaminoglycan attachment site:

amino acids 12-16

N-myristoylation sites:

amino acids 9-15,13-19,15-21,215-221,224-230

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FIGURE 257

CGGACGCGTGGGGCCGT**ATG**CGCGGCTCTGTGGAGTGCACCTGGGGTTGGGGGCACTGTGCCC CCAGCCCCTGCTCCTTTGGACTCTACTTCTGTTTGCAGCCCCATTTGGCCTGCTGGGGGAGA ATATACGGGCAGTGGGCACCAATTCCACACTGCACTATGTGTGGAGCAGCCTGGGGCCTCTGG CAGTGGTAATGGTGGCCACCAACACCCCCCACAGCACCCTGAGCATCAACTGGAGCCTCCTGC TATCCCCTGAGCCCGATGGGGGCCTGATGGTGCTCCCTAAGGACAGCATTCAGTTTTCTTCTG CCCTTGTTTTTACCAGGCTGCTTGAGTTTGACAGCACCAACGTGTCCGATACGGCAGCAAAGC CTTTGGGAAGACCATATCCTCCATACTCCTTGGCCGATTTCTCTTGGAACAACATCACTGATT CATTGGATCCTGCCACCTGAGTGCCACATTTCAAGGCCACCCCATGAACGACCCTACCAGGA CTTTTGCCAATGGCAGCCTGGCCTTCAGGGTCCAGGCCTTTTCCAGGTCCAGCCGACCAGCCC AACCCCCTCGCCTCCTGCACACAGCAGACACCTGTCAGCTAGAGGTGGCCCTGATTGGAGCCT CTCCCGGGGAAACCGTTCCCTGTTTGGGCTGGAGGTAGCCACATTGGGCCAGGGCCCTGACT GCCCCTCAATGCAGGAGCAGCACTCCATCGACGATGAATATGCACCGGCCGTCTTCCAGTTGG ACCAGCTACTGTGGGGCTCCCTCCCATCAGGCTTTGCACAGTGGCGACCAGTGGCTTACTCCC AGAAGCCGGGGGGCCGAGAATCAGCCCTGCCCTGCCAAGCTTCCCCTCTTCATCCTGCCTTAG CATACTCTCTCCCCAGTCACCCATTGTCCGAGCCTTCTTTGGGTCCCAGAATAACTTCTGTG CCTTCAATCTGACGTTCGGGGCTTCCACAGGCCCTGGCTATTGGGACCAACACTACCTCAGCT GGTCGATGCTCCTGGGTGTGGGCTTCCCTCCAGTGGACGCCTTGTCCCCACTAGTCCTGGGCA TCATGGCAGTGGCCCTGGGTGCCCCAGGGCTCATGCTGCTAGGGGGCGGCTTGGTTCTGCTGC TGCACCACAGAGTACTCAGAGTACCAGTCCATAAATTAAGGCCCGCTCTCTGGAGGGAAGG ACATTACTGAACCTGTCTTGCTGTGCCTCGAAACTCTGGAGGTTGGAGCATCAAGTTCCAGCC GGCCCCTTCACTCCCCCATCTTGCTTTTCTGTGGAACCTCAGAGGCCAGCCTCGACTTCCTGG AGACCCCCAGGTGGGGCTTCCTTCATACTTTGTTGGGGGGACTTTGGAGGCGGGCAGGGGACAG GGCTATTGATAAGGTCCCCTTGGTGTTGCCTTCTTGCATCTCCACACATTTCCCTTGGATGGG ACTTGCAGGCCTAAATGAGAGGCATTCTGACTGGTTGGCTGCCCTGGAAGGCAAGAAAATAGA TTTATTTTTTTCACAGGGAAAAAAAAAAA

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FIGURE 258

MRGSVECTWGWGHCAPSPLLLWTLLLFAAPFGLLGEKTRQVSLEVIPNWLGPLQNLLHIRAVG
TNSTLHYVWSSLGPLAVVMVATNTPHSTLSINWSLLLSPEPDGGLMVLPKDSIQFSSALVFTR
LLEFDSTNVSDTAAKPLGRPYPPYSLADFSWNNITDSLDPATLSATFQGHPMNDPTRTFANGS
LAFRVQAFSRSSRPAQPPRLLHTADTCQLEVALIGASPRGNRSLFGLEVATLGQGPDCPSMQE
QHSIDDEYAPAVFQLDQLLWGSLPSGFAQWRPVAYSQKPGGRESALPCQASPLHPALAYSLPQ
SPIVRAFFGSQNNFCAFNLTFGASTGPGYWDQHYLSWSMLLGVGFPPVDGLSPLVLGIMAVAL
GAPGLMLLGGGLVLLLHHKKYSEYQSIN

Important features:

Signal peptide:

amino acids 1-35

Transmembrane domain:

amino acids 365-386

N-glycosylation sites:

amino acids 65-69,95-99,134-138,159-163,187-191,230-234,333-337

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 397-401

N-myristoylation sites:

amino acids 3-9,63-69,235-241,273-279,292-298,324-330

Leucine zipper pattern:

amino acids 371-393

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FIGURE 259

CGTGTCTGCCGTCAACCGCAGGAGGATGAAGCTGCTGCTGGGCATCGCCTTGCTGGCCTACGTCGCCTCTGTTTG GGGCAACTTCGTTAATATGAGGTCTATCCAGGAAAATGGTGAACTAAAAATTGAAAGCAAGATTGAAGAGTGGT TGAACCACTAAGAGAGAAAATCAGAGATTTAGAAAAAAGCTTTACCCAGAAATACCCACCAGTAAAGTTTTTATC AGAAAAGGATCGGAAAAGAATTTTGATAACAGGAGGCGCAGGGTTCGTGGGCTCCCATCTAACTGACAAACTCAT GATGGACGGCCACGAGGTGACCGTGGTGGACAATTTCTTCACGGGCAGGAAGAGAAACGTGGAGCACTGGATCGG ACATGAGAACTTCGAGTTGATTAACCACGACGTGGTGGAGCCCCTCTACATCGAGGTTGACCAGATATACCATCT GGCATCTCCAGCCTCCCAAACTACATGTATAATCCTATCAAGACATTAAAGACCAATACGATTGGGACATT AAACATGTTGGGGCTGGCAAAACGAGTCGGTGCCCGTCTGCTCCTGGCCTCCACATCGGAGGTGTATGGAGATCC TGAAGTCCACCCTCAAAGTGAGGATTACTGGGGCCACGTGAATCCAATAGGACCTCGGGCCTGCTACGATGAAGG ${\tt CAAACGTGTTGCAGAGACCATGTGCTATGCCTACATGAAGCAGGAAGGCGTGGAAGTGCGAGTGGCCAGAATCTT}$ CAACACCTTTGGGCCACGCATGCACATGAACGATGGGCGAGTAGTCAGCAACTTCATCCTGCAGGCGCTCCAGGG GGAGCCACTCACGGTATACGGATCCGGGTCTCAGACAAGGGCGTTCCAGTACGTCAGCGATCTAGTGAATGGCCT CGTGGCTCTCATGAACAGCAACGTCAGCAGCCCGGTCAACCTGGGGAACCCAGAAGAACACACAATCCTAGAATT TGCTCAGTTAATTAAAAACCTTGTTGGTAGCGGAAGTGAAATTCAGTTTCTCTCCGAAGCCCAGGATGACCCACA GAAAAGAAAACCAGACATCAAAAAAGCAAAGCTGATGCTGGGGTGGGAGCCCGTGGTCCCGCTGGAGGAAGGTTT AAACAAAGCAATTCACTACTTCCGTAAAGAACTCGAGTACCAGGCAAATAATCAGTACATCCCCAAACCAAAGCC TGCCAGAATAAAGAAAGGACGGACTCGCCACAGCTGAACTCCTCACTTTTAGGACACAAGACTACCATTGTACAC TGGAATTTCATTCTGAAGCTTGCTTTAATGAAATGGATGTGCCTAAAAGCTCCCCTCAAAAAACTGCAGATTTTG CCTTGCACTTTTTGAATCTCTTTTTTATGTAAAATAGCGTAGATGCATCTCTGCGTATTTTCAAGTTTTTTAT CATTAAGCGGGACAAAAAATGCCGATTTTATTTATAAAAGTGGGTACTTAATAAATGAGTCGTTATACTATGCAT AAAGAAAAATCCTAGCAGTATTGTCAGGTGGTGGTGCGCCGGCATTGATTTTAGGGCAGATAAAAGAATTCTGTG TGAGAGCTTTATGTTTCTCTTTTAATTCAGAGTTTTTCCAAGGTCTACTTTTGAGTTGCAAACTTGACTTTGAAA TATTCCTGTTGGTCATGATCAAGGATATTTGAAATCACTACTGTGTTTTTGCTGCGTATCTGGGGCGGGGGGGAGGT TGGGGGGCACAAGTTAACATATTCTTGGTTAACCATGGTTAAATATGCTATTTTAATAAAATATTGAAACTCA

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FIGURE 260

MVSKALLRLVSAVNRRRMKLLLGIALLAYVASVWGNFVNMRSIQENGELKIESKIEEMVEPLR EKIRDLEKSFTQKYPPVKFLSEKDRKRILITGGAGFVGSHLTDKLMMDGHEVTVVDNFFTGRK RNVEHWIGHENFELINHDVVEPLYIEVDQIYHLASPASPPNYMYNPIKTLKTNTIGTLNMLGL AKRVGARLLLASTSEVYGDPEVHPQSEDYWGHVNPIGPRACYDEGKRVAETMCYAYMKQEGVE VRVARIFNTFGPRMHMNDGRVVSNFILQALQGEPLTVYGSGSQTRAFQYVSDLVNGLVALMNS NVSSPVNLGNPEEHTILEFAQLIKNLVGSGSEIQFLSEAQDDPQKRKPDIKKAKLMLGWEPVV PLEEGLNKAIHYFRKELEYQANNQYIPKPKPARIKKGRTRHS

Important features:

Signal peptide:

amino acids 1-32

N-glycosylation site:

amino acids 316-320

Tyrosine kinase phosphorylation site:

amino acids 235-244

N-myristoylation sites:

amino acids 35-41,101-107,383-389

Amidation sites:

amino acids 123-127,233-237

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FIGURE 261

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FIGURE 262

MALKNKFSCLWILGLCLVATTSSKIPSITDPHFIDNCIEAHNEWRGKVNPPAADMKYMIWDKG LAKMAKAWANQCKFEHNDCLDKSYKCYAAFEYVGENIWLGGIKSFTPRHAITAWYNETQFYDF DSLSCSRVCGHYTQLVWANSFYVGCAVAMCPNLGGASTAIFVCNYGPAGNFANMPPYARGESC SLCSKEEKCVKNLCRTPQLIIPNQNPFLKPTGRAPQQTAFNPFSLGFLLLRIF

Important features:

Signal peptide:

amino acids 1-23

N-glycosylation site:

amino acids 119-123

N-myristoylation sites:

amino acids 103-109,150-156,160-166,161-167,175-181

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 signature 1:

amino acids 136-156

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 signature 2:

amino acids 166-178

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FIGURE 263

CGCCTCCGACCCGCCCCGCGCGCATTGTGGGATCTGTCGGCTTGTCAGGTGGTGGAGGAAA AGGCGCTCCGTCATGGGGATCCAGACGAGCCCCGTCCTGCTGGCCTCCCTGGGGGTGGGGCTG GTCACTCTGCTCGGCCTGTCGGGCTCCTACTTGGTTCGGAGGTCCCGCCGGCCTCAGGTC ACTCTCCTGGACCCCAATGAAAAGTACCTGCTACGACTGCTAGACAAGACGACTGTGAGCCAC AACACCAAGAGGTTCCGCTTTGCCCTGCCCACCGCCCACCACTCTGGGGCTGCCTGTGGGC AAACATATCTACCTCTCCACCCGAATTGATGGCAGCCTGGTCATCAGGCCATACACTCCTGTC ACCAGTGATGAGGATCAAGGCTATGTGGATCTTGTCATCAAGGTCTACCTGAAGGGTGTGCAC CCCAAATTTCCTGAGGGAGGGAAGATGTCTCAGTACCTGGATAGCCTGAAGGTTGGGGATGTG GTGGAGTTTCGGGGGCCAAGCGGGTTGCTCACTTACACTGGAAAAGGGCATTTTAACATTCAG CCCAACAGAATCTCCACCAGAACCCCGAGTGGCGAAGAACTGGGAATGATTGCCGGCGGG ACAGGAATCACCCCAATGCTACAGCTGATCCGGGCCATCCTGAAAGTCCCTGAAGATCCAACC CAGTGCTTTCTGCTTTTTGCCAACCAGACAGAAAAGGATATCATCTTGCGGGAGGACTTAGAG GAACTGCAGGCCCGCTATCCCAATCGCTTTAAGCTCTGGTTCACTCTGGATCATCCCCCAAAA GATTGGGCCTACAGCAAGGGCTTTGTGACTGCCGACATGATCCGGGAACACCTGCCCGCTCCA GGGGATGATGTGCTGGTACTGCTTTGTGGGCCACCCCAATGGTGCAGCTGGCCTGCCATCCC AACTTGGACAAACTGGGCTACTCACAAAAGATGCGATTCACCTAC<u>TGA</u>GCATCCTCCAGCTTC CCTGGTGCTGTTCGCTGCAGTTGTTCCCCATCAGTACTCAAGCACTATAAGCCTTAGATTCCT TTCCTCAGAGTTTCAGGTTTTTCAGTTACATCTAGAGCTGAAATCTGGATAGTACCTGCAGG AACAATATTCCTGTAGCCATGGAAGAGGGCAAGGCTCAGTCACTCCTTGGATGGCCTCCTAAA TCTCCCCGTGGCAACAGGTCCAGGAGAGGCCCATGGAGCAGTCTCTTCCATGGAGTAAGAAGG AAGGGAGCATGTACGCTTGGTCCAAGATTGGCTAGTTCCTTGATAGCATCTTACTCTCACCTT CTTTGTGTCTGTGATGAAAGGAACAGTCTGTGCAATGGGTTTTACTTAAACTTCACTGTTCAA CCTATGAGCAAATCTGTATGTGTGAGTATAAGTTGAGCATAGCATACTTCCAGAGGTGGTNTT ATGGAGATGGCAAGAAAGGAGGAAATGATTTCTTCAGATNTCAAAGGAGTCTGAAATATCATA TTTCTGTGTGTGTCTCTCTCAGCCCCTGCCCAGGCTAGAGGGAAACAGCTACTGATAATCGAA AACTGCTGTTTGTGGCANGAACCCCTGGCTGTGCAAATAAATGGGGCTGAGGCCCCTGTGTGA

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FIGURE 264

MGIQTSPVLLASLGVGLVTLLGLAVGSYLVRRSRRPQVTLLDPNEKYLLRLLDKTTVSHNTKR FRFALPTAHHTLGLPVGKHIYLSTRIDGSLVIRPYTPVTSDEDQGYVDLVIKVYLKGVHPKFP EGGKMSQYLDSLKVGDVVEFRGPSGLLTYTGKGHFNIQPNKKSPPEPRVAKKLGMIAGGTGIT PMLQLIRAILKVPEDPTQCFLLFANQTEKDIILREDLEELQARYPNRFKLWFTLDHPPKDWAY SKGFVTADMIREHLPAPGDDVLVLLCGPPPMVQLACHPNLDKLGYSQKMRFTY

Important features:

Signal peptide:

amino acids 1-26

N-glycosylation site:

amino acids 214-218

N-myristoylation sites:

amino acids 22-28,76-82,128-134,180-186

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FIGURE 265

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACTTGGCTTCGTTAGA ACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACACTATAG AATAACATCCACTTTGCCTTTCTCCACAGGTGTCCACTCCCAGGTCCAACTGCACCTCGGT TCTATCGATAATCTCAGCACCAGCCACTCAGAGCAGGGCACGATGTTGGGGGGCCCGCCTCAGG CTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCGTCCTCAGAGCCTATCCCAATGCC TCCCCACTGCTCGGCTCCAGCTGGGGTGGCCTGATCCACCTGTACACAGCCACAGCCAGGAAC AGCTACCACCTGCAGATCCACAAGAATGGCCATGTGGATGGCGCACCCCATCAGACCATCTAC AGTGCCCTGATGATCAGATCAGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGATGAGCAGA AGATACCTCTGCATGGATTTCAGAGGCAACATTTTTGGATCACACTATTTCGACCCGGAGAAC TGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCCTCAGTATCAC TCCCAGTTCCTGTCCCGGAGGAACGAGATCCCCCTAATTCACTTCAACACCCCCATACCACGG CGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCCTGAACGTGCTGAAGCCCCGG GCCCGGATGACCCCGGCCCCGGCCTCTGTTCACAGGAGCTCCCGAGCGCCGAGGACAACAGC ACGGGCCCGGAAGGCTGCCGCCCCTTCGCCAAGTTCATCTAGGGTCGCTGG

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FIGURE 266

MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGGLIHLYTATARNSYHLQIHKNGHVDG APHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTLENGYDV YHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTPIPRRHTRSAEDDSERDP LNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFAKFI

Important features:

Signal peptide:

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 175-179

N-myristoylation site.

amino acids 33-39, 100-106, 225-231, 229-235

HBGF/FGF family proteins

amino acids 73-124

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FIGURE 267

AGCCAACCAGGGTCAGGCTGTGCTCACAGTTTCCTCTGGCGGCATGTAAAGGCTCCACAAAGGAGTTGGGAGTTC AAATGAGGCTGCTGCGGACGGCCTGAGGATGGACCCCAAGCCCTGGACCTGCCGAGCGTGGCACTGAGGCAGCGG CTGACGCTACTGTGAGGGAAAGAAGGTTGTGAGCAGCCCCGCAGGACCCCTGGCCAGCCCTGGCCCAGCCTCTG $\tt CCGGAGCCCTCTGTGGAGGCAGAGCCAGTGGAGCCCAGTGAGGCAGGGCTGCTTGGCAGCCACCGGCCTGCAACT$ CAGGAACCCCTCCAGAGGCCATGGACAGGCTGCCCCGCTGACGGCCAGGGTGAAGCATGTGAGGAGCCGCCCCGG AAGTGCACCTACACCTTCATTGTGCCCCAGCAGCGGGTCACGGGTGCCATCTGCGTCAACTCCAAGGAGCCTGAG GTGCTTCTGGAGAACCGAGTGCATAAGCAGGAGCTAGAGCTGCTCAACAATGAGCTGCTCAAGCAGAAGCGGCAG ATCGAGACGCTGCAGCAGCTGGTGGAGGTGGACGGCGGCATTGTGAGCGAGGTGAAGCTGCTGCGCAAGGAGAGC CGCAACATGAACTCGCGGGTCACGCAGCTCTACATGCAGCTCCTGCACGAGATCATCCGCAAGCGGGACAACGCG TTGGAGCTCTCCCAGCTGGAGAACAGGATCCTGAACCAGACAGCCGACATGCTGCAGCTGGCCAGCAAGTACAAG GAGCTGGAGCACAAGTACCAGCACCTGGCCACACTGGCCCACAACCAATCAGAGATCATCGCGCAGCTTGAGGAG CCCACCTACAACCGCATCATCAACCAGATCTCTACCAACGAGATCCAGAGTGACCAGAACCTGAAGGTGCTGCCA CCCCCTCTGCCCACTATGCCCACTCTCACCAGCCTCCCATCTTCCACCGACAAGCCGTCGGGCCCATGGAGAGAC TGCCTGCAGGCCCTGGAGGATGGCCACGACACCAGCTCCATCTACCTGGTGAAGCCGGAGAACACCAACCGCCTC ATGCAGGTGTGCGACCAGAGACACGACCCCGGGGGCTGGACCGTCATCCAGAGACGCCTGGATGGCTCTGTT AACATTTACTGGCTGACGAACCAAGGCAACTACAAACTCCTGGTGACCATGGAGGACTGGTCCGGCCGCAAAGTC TTTGCAGAATACGCCAGTTTCCGCCTGGAACCTGAGAGCGAGTATTATAAGCTGCGGCTGGGGCGCTACCATGGC AATGCGGGTGACTCCTTTACATGGCACAACGGCAAGCAGTTCACCACCCTGGACAGAGTCATGATGTCTACACA GGAAACTGTGCCCACTACCAGAAGGGAGGCTGGTGGTATAACGCCTGTGCCCACTCCAACCTCAACGGGGTCTGG TACCGCGGGGCCATTACCGGAGCCGCTACCAGGACGGAGTCTACTGGGCTGAGTTCCGAGGAGGCTCTTACTCA $\tt CTCAAGAAAGTGGTGATGATCCGACCGAACCCCAACACCTTCCAC{\color{red}{TAA}} GCCAGCTCCCCCTCCTGACCTCTC$ GTGGCCATTGCCAGGAGCCCACCCTGGTCACGCTGGCCACAGCACAAGAACAACTCCTCACCAGTTCATCCTGA GGCTGGGAGGACCGGGATGCTGGATTCTGTTTTCCGAAGTCACTGCAGCGGATGATGGAACTGAATCGATACGGT GTTTTCTGTCCCTCCTACTTCACACCAGACAGCCCCTCATGTCTCCCAGGACAGGACAGGACTACAGACAA CTCTTTCTTTAAATAAATTAAGTCTCTACAATAAAAAAA

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FIGURE 268

MRPLCVTCWWLGLLAAMGAVAGQEDGFEGTEEGSPREFIYLNRYKRAGESQDKCTYTFIVPQQ
RVTGAICVNSKEPEVLLENRVHKQELELLNNELLKQKRQIETLQQLVEVDGGIVSEVKLLRKE
SRNMNSRVTQLYMQLLHEIIRKRDNALELSQLENRILNQTADMLQLASKYKDLEHKYQHLATL
AHNQSEIIAQLEEHCQRVPSARPVPQPPPAAPPRVYQPPTYNRIINQISTNEIQSDQNLKVLP
PPLPTMPTLTSLPSSTDKPSGPWRDCLQALEDGHDTSSIYLVKPENTNRLMQVWCDQRHDPGG
WTVIQRRLDGSVNFFRNWETYKQGFGNIDGEYWLGLENIYWLTNQGNYKLLVTMEDWSGRKVF
AEYASFRLEPESEYYKLRLGRYHGNAGDSFTWHNGKQFTTLDRDHDVYTGNCAHYQKGGWWYN
ACAHSNLNGVWYRGGHYRSRYQDGVYWAEFRGGSYSLKKVVMMIRPNPNTFH

Important features:

Signal peptide:

amino acids 1-22

N-glycosylation sites:

amino acids 164-168,192-196

cAMP- and cGMP-dependent protein kinase phosphorylation site: amino acids 124-128

Tyrosine kinase phosphorylation sites:

amino acids 177-184,385-393,385-394,461-468

N-myristoylation sites:

amino acids 12-18,18-24,22-28,29-35,114-120,341-347,465-471,473-479

Amidation site:

amino acids 373-377

Fibrinogen beta and gamma chains C-terminal domain signature:

amino acids 438-451

Fibrinogen beta and gamma chains C-terminal domain proteins: amino acids 305-343, 365-402, 411-424, 428-458

Trehalase proteins:

amino acids 275-292

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FIGURE 269

GCCGAGCTGAGCGGATCCTCACATGACTGTGATCCGATTCTTTCCAGCGGCTTCTGCAACCAA GCGGGTCTTACCCCCGGTCCTCCGCGTCTCCAGTCCTCGCACCTGGAACCCCAACGTCCCCGA GAGTCCCCGAATCCCCGCTCCCAGGCTACCTAAGAGGATGAGCGGTGCTCCGACGGCCGGGGC AGCCCTGATGCTCTGCGCCGCCACCGCCGTGCTACTGAGCGCTCAGGGCGGACCCGTGCAGTC CAAGTCGCCGCGCTTTGCGTCCTGGGACGAGATGAATGTCCTGGCGCACGGACTCCTGCAGCT CGGCCAGGGGCTGCGCGAACACGCGGAGCGCACCCGCAGTCAGCTGAGCGCGCTGGAGCGGCG CCTGAGCGCGTGCGGGTCCGCCTGTCAGGGAACCGAGGGGTCCACCGACCTCCCGTTAGCCCC TGAGAGCCGGGTGGACCCTGAGGTCCTTCACAGCCTGCAGACACACTCAAGGCTCAGAACAG CAGGATCCAGCAACTCTTCCACAAGGTGGCCCAGCAGCAGCAGCACCTGGAGAAGCAGCACCT GCGAATTCAGCATCTGCAAAGCCAGTTTGGCCTCCTGGACCACAAGCACCTAGACCATGAGGT TGTCAGCCGCCTGCACCGGCTGCCCAGGGATTGCCAGGAGCTGTTCCAGGTTGGGGAGAGGCA GAGTGGACTATTTGAAATCCAGCCTCAGGGGTCTCCGCCATTTTTTGGTGAACTGCAAGATGAC CTCAGATGGAGGCTGGACAGTAATTCAGAGGCGCCACGATGGCTCAGTGGACTTCAACCGGCC GGTGCATAGCATCACGGGGGACCGCAACAGCCGCCTGGCCGTGCAGCTGCGGGACTGGGATGG CAACGCCGAGTTGCTGCAGTTCTCCGTGCACCTGGGTGGCGAGGACACGGCCTATAGCCTGCA ACCCTTCTCCACTTGGGACCAGGATCACGACCTCCGCAGGGACAAGAACTGCGCCAAGAGCCT CTCTGGAGGCTGGTGGTTTGGCACCTGCAGCCATTCCAACCTCAACGGCCAGTACTTCCGCTC CATCCCACAGCAGCAGCAGAAGCTTAAGAAGGGAATCTTCTGGAAGACCTGGCGGGCCGCTA CTACCCGCTGCAGGCCACCATGTTGATCCAGCCCATGGCAGCAGAGGCAGCCTCC**TAG**CG TCCTGGCTGGCCTGGTCCCAGGCCCACGAAAGACGGTGACTCTTGGCTCTGCCCGAGGATGT GGCCGTTCCCTGCCTGGGCAGGGGCTCCAAGGAGGGGCCATCTGGAAACTTGTGGACAGAGAA GAAGACCACGACTGGAGAAGCCCCCTTTCTGAGTGCAGGGGGGGCTGCATGCGTTGCCTCCTGA GATCGAGGCTGCAGGATATGCTCAGACTCTAGAGGCGTGGACCAAGGGGCATGGAGCTTCACT TGGCGGACTCAGTCACATTGACTGACGGGGACCAGGGCTTGTGTGGGTCGAGAGCGCCCTCAT GGTGCTGGTGCTGTTGTGTGTGTGGGCCCCTGGGGACACAAGCAGGCGCCCAATGGTATCTGGGC GGAGCTCACAGAGTTCTTGGAATAAAAGCAACCTCAGAACAC

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FIGURE 270

MTVIRFFPAASATKRVLPPVLRVSSPRTWNPNVPESPRIPAPRLPKRMSGAPTAGAALMLCAA TAVLLSAQGGPVQSKSPRFASWDEMNVLAHGLLQLGQGLREHAERTRSQLSALERRLSACGSA CQGTEGSTDLPLAPESRVDPEVLHSLQTQLKAQNSRIQQLFHKVAQQQRHLEKQHLRIQHLQS QFGLLDHKHLDHEVAKPARRKRLPEMAQPVDPAHNVSRLHRLPRDCQELFQVGERQSGLFEIQ PQGSPPFLVNCKMTSDGGWTVIQRRHDGSVDFNRPWEAYKAGFGDPHGEFWLGLEKVHSITGD RNSRLAVQLRDWDGNAELLQFSVHLGGEDTAYSLQLTAPVAGQLGATTVPPSGLSVPFSTWDQ DHDLRRDKNCAKSLSGGWWFGTCSHSNLNGQYFRSIPQQRQKLKKGIFWKTWRGRYYPLQATT MLIQPMAAEAAS

Important features:

Signal peptide:

Amino acids 1-13

Transmembrane domain:

Amino acids 53-70

N-glycosylation site:

Amino acids 224-228

cAMP- and cGMP-dependent protein kinase phosphorylation sites: Amino acids 46-50;118-122

N-myristoylation sites:

Amino acids 50-56;129-135;341-347;357-363

Fibrinogen beta and gamma chains C-terminal domain signature:

Amino acids 396-409

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FIGURE 271

CGGACGCGTGGGGGAAACCCTTCCGAGAAAACAGCAACAAGCTGAGCTGCTGTGACAGAGGGG AACAAG<u>ATG</u>GCGGCGCCGAAGGGGAGCCTCTGGGTGAGGACCCAACTGGGGCTCCCGCCGCTG CTGCTGCTGACCATGGCCTTGGCCGGAGGTTCGGGGACCGCTTCGGCTGAAGCATTTGACTCG GTCTTGGGTGATACGGCGTCTTGCCACCGGGCCTGTCAGTTGACCTACCCCTTGCACACCTAC CCTAAGGAAGAGGGTTGTACGCATGTCAGAGGGTTGCAGGCTGTTTTCAATTTGTCAGTTT GTGGATGATGGAATTGACTTAAATCGAACTAAATTGGAATGTGAATCTGCATGTACAGAAGCA TATTCCCAATCTGATGAGCAATATGCTTGCCATCTTGGTTGCCAGAATCAGCTGCCATTCGCT GAACTGAGACAAGAACAACTTATGTCCCTGATGCCAAAAATGCACCTACTCTTTCCTCTAACT CTGGTGAGGTCATTCTGGAGTGACATGATGGACTCCGCACAGAGCTTCATAACCTCTTCATGG ACTTTTTATCTTCAAGCCGATGACGGAAAAATAGTTATATTCCAGTCTAAGCCAGAAATCCAG TACGCACCACATTTGGAGCAGGAGCCTACAAATTTGAGAGAATCATCTCTAAGCAAAATGTCC TATCTGCAAATGAGAAATTCACAAGCGCACAGGAATTTTCTTGAAGATGGAGAAAGTGATGGC TTTTTAAGATGCCTCTCTTAACTCTGGGTGGATTTTAACTACAACTCTTGTCCTCTCGGTG ATGGTATTGCTTTGGGATTTGTTGTGCAACTGTTGCTACAGCTGTGGAGCAGTATGTTCCCTCT GCTTCTTCTCTTGTGGTTGTTAGATCTAAAACTGAAGATCATGAAGAAGCAGGGCCTCTACCT ACAAAAGTGAATCTTGCTCATTCTGAAATT**TAA**GCATTTTTCTTTTAAAAGACAAGTGTAATA GACATCTAAAATTCCACTCCTCATAGAGCTTTTAAAATGGTTTCATTGGATATAGGCCTTAAG AAATCACTATAAAATGCAAATAAAGTTACTCAAATCTGTG

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FIGURE 272

MAAPKGSLWVRTQLGLPPLLLLTMALAGGSGTASAEAFDSVLGDTASCHRACQLTYPLHTYPK
EEELYACQRGCRLFSICQFVDDGIDLNRTKLECESACTEAYSQSDEQYACHLGCQNQLPFAEL
RQEQLMSLMPKMHLLFPLTLVRSFWSDMMDSAQSFITSSWTFYLQADDGKIVIFQSKPEIQYA
PHLEQEPTNLRESSLSKMSYLQMRNSQAHRNFLEDGESDGFLRCLSLNSGWILTTTLVLSVMV
LLWICCATVATAVEQYVPSEKLSIYGDLEFMNEQKLNRYPASSLVVVRSKTEDHEEAGPLPTK
VNLAHSEI

Important features:

Signal peptide:

amino acids 1-31

Transmembrane domain:

amino acids 241-260

N-glycosylation site:

amino acids 90-94

N-myristoylation sites:

amino acids 28-34,29-35,31-37,86-92

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FIGURE 273

 $\verb|CCCACGCGTCCGAACCTCTCCAGCG| \textbf{ATC} \\ \texttt{GGAGCCGCCCGCCTGCTGCCCAACCTCACTCTGTG} \\$ CTTACAGCTGCTGATTCTCTGCTGTCAAACTCAGTACGTGAGGGACCAGGGCGCCATGACCGA CCAGCTGAGCAGGCGGCAGATCCGCGAGTACCAACTCTACAGCAGGACCAGTGGCAAGCACGT GCAGGTCACCGGGGGTCGCATCTCCGCCACCGCGAGGACGGCAACAAGTTTGCCAAGCTCAT AGTGGAGACGGACACGTTTGGCAGCCGGGTTCGCATCAAAGGGGGCTGAGAGTGAGAAGTACAT CTGTATGAACAAGAGGGGCAAGCTCATCGGGAAGCCCAGCGGGAAGAGCAAAGACTGCGTGTT CACGGAGATCGTGCTGGAGACAACTATACGGCCTTCCAGAACGCCCGGCACGAGGGCTGGTT CATGGCCTTCACGCGGCAGGGGCGGCCCGCCAGGCTTCCCGCAGCCGCCAGAACCAGCGCGA GGCCCACTTCATCAAGCGCCTCTACCAAGGCCAGCTGCCCTTCCCCAACCACGCCGAGAAGCA GAAGCAGTTCGAGTTTGTGGGCTCCGCCCCACCCGCCGGACCAAGCGCACACGGCGGCCCCA GCCCCTCACGTAGTCTGGGAGGCAGGGGGCAGCAGCCCCTGGGCCGCCTCCCCACCCCTTTCC TGAGGGCCGCGAAGCATCCGAGCCCCCAGCTGGGAAGGGGCAGGCCGGTGCCCCAGGGGCCGC TGGCACAGTGCCCCCTTCCCGGACGGGTGGCAGGCCCTGGAGAGGAACTGAGTGTCACCCTGA TCTCAGGCCACCAGCCTCTGCCGGCCTCCCAGCCGGGCTCCTGAAGCCCGCTGAAAGGTCAGC GACTGAAGGCCTTGCAGACAACCGTCTGGAGGTGGCTGTCCTCAAAATCTGCTTCTCGGATCT CCCTCAGTCTGCCCCCAGCCCCCAAACTCCTCCTGGCTAGACTGTAGGAAGGGACTTTTGTTT CATTCCACGACCCAGGCCTGCACCCCCAACTCCCAGCCCCGGAATAAAACCATTTTCC TGC

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FIGURE 274

MGAARLLPNLTLCLQLLILCCQTQYVRDQGAMTDQLSRRQIREYQLYSRTSGKHVQVTGRRIS ATAEDGNKFAKLIVETDTFGSRVRIKGAESEKYICMNKRGKLIGKPSGKSKDCVFTEIVLENN YTAFQNARHEGWFMAFTRQGRPRQASRSRQNQREAHFIKRLYQGQLPFPNHAEKQKQFEFVGS APTRRTKRTRRPOPLT

Important features:

Signal peptide:

Amino acids 1-22

N-glycosylation site.

amino acids 9-13, 126-130

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 60-64

Casein kinase II phosphorylation site.

amino acids 65-69

Tyrosine kinase phosphorylation site.

amino acids 39-48, 89-97

N-myristoylation site.

amino acids 69-75, 188-194

Amidation site.

amino acids 58-62

HBGF/FGF family signature.

amino acids 103-128

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FIGURE 275

TATTTACCATATCAGATTCACATTCAGTCCTCAGCAAAATGAAGGGCTCCATTTTCACTCTGT
TTTTATTCTCTGTCCTATTTGCCATCTCAGAAGTGCGGAGCAAGGAGTCTGTGAGACTCTGTG
GGCTAGAATACATACGGACAGTCATCTATATCTGTGCTAGCTCCAGGTGGAGAAGGCATCTGG
AGGGGATCCCTCAAGCTCAGCAAGCTGAGACAGGAAACTCCTTCCAGCTCCCACATAAACGTG
AGTTTTCTGAGGAAAATCCAGCGCAAAACCTTCCGAAGGTGGATGCCTCAGGGGAAGACCGTC
TTTGGGGTGGACAGATGCCCACTGAAGAGCTTTGGAAGTCAAAGAAGCATTCAGTGATGTCAA
GACAAGATTTACAAACTTTGTGTTGCACTGATGGCTGTTCCATGACTGATTTGAGTGCTCTTT
GCTAAGACAAGAGCAAATACCCAATGGGTGGCAGAGCTTTATCACATGTTTTAATTACAGTGTT
TTACTGCCTGGTAGAACACTAATATTGTGTTATTAAAATGATGGCTTTTTGGGTAGGCAAAACT
TCTTTTCTAAAAAGGTATAGCTGAGCCGTTGAAACCACAGTGATCTCTATTTTCTCCCTTTGCC
AAGGTTAATGAACTGTTCTTTTCAAATTCTACTAATGCTTTGAAATTTCAAATGCTGCGCAAA
ATTGCAATAAAAAATGCTATAAA

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FIGURE 276

MKGSIFTLFLFSVLFAISEVRSKESVRLCGLEYIRTVIYICASSRWRRHLEGIPQAQQAETGN SFQLPHKREFSEENPAQNLPKVDASGEDRLWGGQMPTEELWKSKKHSVMSRQDLQTLCCTDGC SMTDLSALC

Important features:

Signal sequence:

amino acids 1-18

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 107-111

N-myristoylation sites:

amino acids 3-9,52-58,96-102,125-131

Insulin family signature:

amino acids 121-136

Insulin family proteins:

amino acids 28-46

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FIGURE 277

GCAGCTGGTTACTGCATTTCTCCATGTGGCAGACAGAGCCACAACGCTTTCTCTGCTGGATTAAAGACGG CCCACAGACCAGAACTTCCACTATACTACTTAAAATTACATAGGTGGCTTGTCAAATTCAATTGATTAGTATTGT AAAAGGAAAAAGAAGTTCCTTCTTACAGCTTGGATTCAACGGTCCAAAACAAAAATGCAGCTGCCATTAAAGTCT CAGATGAACAAACTTCTACACTGATTTTTAAAATCAAGAATAAGGGCAGCAAGTTTCTGGATTCACTGAATCAAC AGACACAAAAAGCTGGCAATATAGCAACTATGAAGAGAAAAGCTACTAATAAAATTAACCCAACGCATAGAAGAC QAAGACTTTTACCTGGACCCTAGGTGTGCTATTCTTCCTACTAGTGGACACTGGACATTGCAGAGGTGGACAATT CAAAATTAAAAAAATAAACCAGAGAAGATACCCTCGTGCCACAGATGGTAAAGAGGAAGCAAAGAAATGTGCATA CACATTCCTGGTACCTGAACAAAGAATAACAGGGCCAATCTGTGTCAACACCAAGGGGCAAGATGCAAGTACCAT TCTGCAACTGGTGGTGGATGTAGATGGAAACATTGTGAATGAGGTAAAGCTGCTGAGAAAGGAAAGCCGTAACAT GAACTCTCGTGTTACTCAACTCTATATGCAATTATTACATGAGATTATCCGTAAGAGGGGATAATTCACTTGAACT TTCCCAACTGGAAAACAAAATCCTCAATGTCACCACAGAAATGTTGAAGATGGCAACAAGATACAGGGAACTAGA GGTGAAATACGCTTCCTTGACTGATCTTGTCAATAACCAATCTGTGATGATCACTTTGTTGGAAGAACAGTGCTT GAGGATATTTTCCCGACAAGACACCCATGTGTCCCCCCACTTGTCCAGGTGGTGCCACAACATATTCCTAACAG CCAACAGTATACTCCTGGTCTGCTGGGAGGTAACGAGATTCAGAGGGATCCAGGTTATCCCAGAGATTTAATGCC ACCACCTGATCTGGCAACTTCTCCCACCAAAAGCCCTTTCAAGATACCACCGGTAACTTTCATCAATGAAGGACC ATTCAAAGACTGTCAGCAAGCAAAAGAAGCTGGGCATTCGGTCAGTGGGATTTATATGATTAAACCTGAAAAACAG CAATGGACCAATGCAGTTATGGTGTGAAAACAGTTTGGACCCTGGGGGTTGGACTGTTATTCAGAAAAGAACAGA CGGCTCTGTCAACTTCTCAGAAATTGGGAAAATTATAAGAAAGGGTTTGGAAACATTGACGGAGAATACTGGCT TAAAAAAGTCTATGCAGAATACAGCAGCTTTCGTCTGGAACCTGAAAGTGAATTCTATAGACTGCGCCTGGGAAC TTACCAGGGAAATGCAGGGGATTCTATGATGTGGCATAATGGTAAACAATTCACCACACTGGACAGAGATAAAGA TATGTATGCAGGAAACTGCGCCCACTTTCATAAAGGAGGCTGGTGGTACAATGCCTGTGCACATTCTAACCTAAA TGGAGTATGGTACAGAGGGCCATTACAGAAGCACGACCAAGATGGAATTTTCTGGGCCGAATACAGAGGCGG ${\tt GTCATACTCCTTAAGAGCAGTTCAGATGATGATCAAGCCTATTGAC} {\tt TGA} {\tt AGAGAGACACTCGCCAATTTAAATGA}$ ACAGAAAGTTTTTAAAATGAATTTTACCGTAACTATAAAAGGGAACCTATAAATGTAGTTTCATCTGTCGTCAAT CTTAACAATTTATTTAAAATCTAAGATTGCTCTAACGTCTAGTGAAAAAAATATTTTTTAAATTTCAGCCAAATA ATGCATTTTATTATAAAAATACAGACAGAAAATTAGGGAGAAACTTCTAGTTTTGCCAATAGAAAATGTTCTT CCATTGAATAAAAGTTATTTCAAATTGAATTTGTGCCTTTCACACGTAATGATTAAATCTGAATTCTTAATAATA CATATGATATGCTGAACACCAAAATCTCCAGAAATGCATTTTATGTAGTTCTAAAATCAGCAAAATATTGGTATT ACTGATCTTACTACTACAAAGAAAAAAAACCCAACCCATCTGCAATTCAAATCAGAAAGTTTGGACAGCTTTAC GAATTCAACAGCTCCAGAGCAGAAGCCACAGGGGCATAGCTTAGTCCAAACTGCTAATTTCATTTTACAGTGTAT GTAACGCTTAGTCTCACAGTGTCTTTAACTCATCTTTGCAATCAACAACTTTACTAGTGACTTTCTGGAACAACT TCCTTTCAGGAATACATATTCACTGCTTAGAGGTGACCTTGCCTTAATATATTTGTGAAGTTAAAATTTTAAAGA TAGCTCATGAAACTTTTGCTTAAGCAAAAAGAAAACCTCGAATTGAAATGTGTGAGGCAAACTATGCATGGGAAT AGCTTAATGTGAAGATAATCATTTGGACAACTCAAATCCATCAACATGACCAATGTTTTTCATCTGCCACATCTC AAAATAAAACTTCTGGTGAAACAAATTAAACAAAATATCCAAACCTCAAAAAAA

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FIGURE 278

MKTFTWTLGVLFFLLVDTGHCRGGQFKIKKINQRRYPRATDGKEEAKKCAYTFLVPEQRITGP
ICVNTKGQDASTIKDMITRMDLENLKDVLSRQKREIDVLQLVVDVDGNIVNEVKLLRKESRNM
NSRVTQLYMQLLHEIIRKRDNSLELSQLENKILNVTTEMLKMATRYRELEVKYASLTDLVNNQ
SVMITLLEEQCLRIFSRQDTHVSPPLVQVVPQHIPNSQQYTPGLLGGNEIQRDPGYPRDLMPP
PDLATSPTKSPFKIPPVTFINEGPFKDCQQAKEAGHSVSGIYMIKPENSNGPMQLWCENSLDP
GGWTVIQKRTDGSVNFFRNWENYKKGFGNIDGEYWLGLENIYMLSNQDNYKLLIELEDWSDKK
VYAEYSSFRLEPESEFYRLRLGTYQGNAGDSMMWHNGKQFTTLDRDKDMYAGNCAHFHKGGWW
YNACAHSNLNGVWYRGGHYRSKHQDGIFWAEYRGGSYSLRAVQMMIKPID

Important features:

Signal sequence:

Amino acids 1-23

N-glycosylation sites:

Amino acids 160-164;188-192

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 120-124

Tyrosine kinase phosphorylation sites:

Amino acids 173-180;387-396

N-myristoylation sites:

Amino acids 70-76;110-116;232-238,343-349;400-406;467-473; 475-487

Fibrinogen beta and gamma chains C-terminal domain signature:

Amino acids 440-453

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FIGURE 279

CCCACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCCTGCCAGTCTCGCCCGCGATCCCGGC CCGGAGGAGCTCGGACGCATGCTGAGCCCCCTCCTTTGCTGAAGCCCGAGTGCGGAGAAGCC CGGGCAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAGCGGA TGGCCATGGCGGCGGCTATCGCCAGCTCGCTCATCCGTCAGAAGAGGCAAGCCCGCGAGCGCG AGAAATCCAACGCCTGCAAGTGTGTCAGCAGCCCCAGCAAAGGCAAGACCAGCTGCGACAAAA ACAAGTTAAATGTCTTTTCCCGGGTCAAACTCTTCGGCTCCAAGAAGAGGCGCAGAAGAAGAC CAGAGCCTCAGCTTAAGGGTATAGTTACCAAGCTATACAGCCGACAAGGCTACCACTTGCAGC TGCAGGCGGATGGAACCATTGATGGCACCAAAGATGAGGACAGCACTTACACTCTGTTTAACC TCATCCCTGTGGGTCTGCGAGTGGTGGCTATCCAAGGAGTTCAAACCAAGCTGTACTTGGCAA TGAACAGTGAGGGATACTTGTACACCTCGGAACTTTTCACACCTGAGTGCAAATTCAAAGAAT CAGTGTTTGAAAATTATTATGTGACATATTCATCAATGATATACCGTCAGCAGCAGTCAGGCC GAGGGTGGTATCTGGGTCTGAACAAAGAAGGAGAGATCATGAAAGGCAACCATGTGAAGAAGA ACAAGCCTGCAGCTCATTTTCTGCCTAAACCACTGAAAGTGGCCATGTACAAGGAGCCATCAC CTGGCGTGCTGAACGGAGGCAAATCCATGAGCCACAATGAATCAACG**TAG**CCAGTGAGGGCAA AAGAAGGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAATTCTTCTAGCAGTCCTTCA TGCCATTAGACCTTCTTATCATCCATACTAAAGC

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FIGURE 280

MAAAIASSLIRQKRQAREREKSNACKCVSSPSKGKTSCDKNKLNVFSRVKLFGSKKRRRRRPE PQLKGIVTKLYSRQGYHLQLQADGTIDGTKDEDSTYTLFNLIPVGLRVVAIQGVQTKLYLAMN SEGYLYTSELFTPECKFKESVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVKKNK PAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKSRSVSGVLNGGKSMSHNEST

Important Features:

N-glycosylation site:

Amino acids 242-246

Glycosaminoglycan attachment sites:

Amino acids 165-169, 218-222

Tyrosine kinase phosphorylation site:

Amino acids 93-100

N-myristoylation sites:

Amino acids 87-93, 231-237

ATP/GTP-binding site motif A (P-loop):

Amino acids 231-239

HBGF/FGF family proteins:

Amino acids 78-94, 102-153

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FIGURE 281

CCAGGATGGAGCTGGGGCCTGTATAGCCATATTATTGTTCTATGCTACTAGACATGGGGGGGA CTTGGTGAAAAAGGTATTATCCAGCCAGAGGGTCTGGGGAGCCCTGTCTTACTGAACCTGGGCA ACCTGGATATTCTGAGACATATTTTGGGGGGGATTCCAGTGAAAAAAGTGGGGGATCCCCTCCA AGTAGGGGTGGGATGAGCGAATATTCCCAAAGCTAAAGTCCCACACCCTGTAGATTACAAGAG TGGATTTGGCAGGAGTGTGCCCCAAAATACAGTGGAAAGGTGCCTGAAGATATTTAAACCACG GGGAAAGGGGACGTTTTCAATAGGAGGCAAAACTCGAGGGTGGGATCCACTGAGGAGTACATA GGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCCACGGGTGGTAACTGGCTGCTGTGGAGGGG CCTGAGCGTCAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGGGAGCCCAGCGCGCTCCGGG CGCCTGCCGGTTTGGGGGTGTCTCCTCCCGGGGCGCTATGGCGCGCTGGCCAGTAGCCTGAT GTGTCCCCGCGGCACCAAGTCCCTTTGCCAGAAGCAGCTCCTCATCCTGCTGTCCAAGGTGCG ACTGTGCGGGGGCCGCCCGCGCCGGCCGGCCCGGAGCCTCAGCTCAAAGGCATCGT CACCAAACTGTTCTGCCGCCAGGGTTTCTACCTCCAGGCGAATCCCGACGGAAGCATCCAGGG CACCCAGAGGATACCAGCTCCTTCACCCACTTCAACCTGATCCCTGTGGGCCTCCGTGTGGT CACCATCCAGAGCGCCAAGCTGGGTCACTACATGGCCATGAATGCTGAGGGACTGCTCTACAG TTCGCCGCATTTCACAGCTGAGTGTCGCTTTAAGGAGTGTGTCTTTGAGAATTACTACGTCCT GTACGCCTCTGCTCTCTACCGCCAGCGTCGTTCTGGCCGGGCCTGGTACCTCGGCCTGGACAA GGAGGGCCAGGTCATGAAGGGAAACCGAGTTAAGAAGACCAAGGCAGCTGCCCACTTTCTGCC CAAGCTCCTGGAGGTGGCCATGTACCAGGAGCCTTCTCTCCACAGTGTCCCCGAGGCCTCCCC TTCCAGTCCCCTGCCCCCTGAAATGTAGTCCCTGGACTGGAGGTTCCCTGCACTCCCAGTGA GCCAGCCACCACAACCTGT

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FIGURE 282

MAALASSLIRQKREVREPGGSRPVSAQRRVCPRGTKSLCQKQLLILLSKVRLCGGRPARPDRG PEPQLKGIVTKLFCRQGFYLQANPDGSIQGTPEDTSSFTHFNLIPVGLRVVTIQSAKLGHYMA MNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNRVKK TKAAAHFLPKLLEVAMYQEPSLHSVPEASPSSPPAP

Important features:

Tyrosine kinase phosphorylation site:

Amino acids 199-207

N-myristoylation sites:

Amino acids 54-60; 89-95; 131-137

HBGF/FGF family signature:

Amino acids 131-155

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FIGURE 283

ATGCCCGCGCCATCGCTAGCGGCTTGATCCGCCAGAAGCGGCAGGCGGGAGCAGCACTGG
GACCGGCCGTCTGCCAGCAGGAGGCGGAGCAGCCCCAGCAAGAACCGCGGGCTCTGCAACGGC
AACCTGGTGGATATCTTCTCCAAAGTGCGCATCTTCGGCCTCAAGAAGCGCAGGTTGCGGCGC
CAAGATCCCCAGCTCAAGGGTATAGTGACCAGGTTATATTGCAGGCAAGGCTACTACTTGCAA
ATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCTTCAAC
CTCATACCAGTGGGACTACGTGTTGTTGCCATCCAGGGAGTGAAAACAGGGTTGTATATAGCC
ATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTTACCCCTGAATGCAAGTTTAAAGAA
TCTGTTTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGGAATCTGGT
AGAGCCTGGTTTTTGGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACCAGCATCT
TTGCATGATGTTGGGGAAACCGTCCCGAAGCCATTGGAAGTTGCCATGTACCGAGAACCATCT
TTGCATGATGTTGGGGAAACCGGTCCCGAAGCCTGGGGTGACGCCAAGTAAAAGCACAAGTGCG
TCTGCAATAATGAATGGAGGCAAACCAGTCAACAAGAGTAAAGACAACATAG

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FIGURE 284

MAAAIASGLIRQKRQAREQHWDRPSASRRRSSPSKNRGLCNGNLVDIFSKVRIFGLKKRRLRR QDPQLKGIVTRLYCRQGYYLQMHPDGALDGTKDDSTNSTLFNLIPVGLRVVAIQGVKTGLYIA MNGEGYLYPSELFTPECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNRVKK TKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKSKTT

Important features:

N-glycosylation sites:

Amino acids 100-104, 242-246

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 28-32, 29-33

Tyrosine kinase phosphorylation site:

Amino acids 199-207

N-myristoylation sites:

Amino acids 38-44, 89-95, 118-124, 122-128, 222-228

HBGF/FGF family proteins:

Amino acids 104-155, 171-198

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FIGURE 285

TCCTTTTCAAAAACTGGAGACACAGAAGAGGGCTCTAGGAAAAAGTTTTGGATGGGATTATGTGGAAACTACCCT GCGATTCTCTGCTGCCAGAGCAGGCTCGGCGCTTCCACCCCAGTGCAGCCTTCCCCTGGCGGTGGTGAAAGAGAC ${\tt TCGGGAGTCGCTGCTTCCAAAGTGCCCGCCGTGAGTGAGCTCTCACCCCAGTCAGCCAA} {\tt ATG} {\tt AGCCTCTTCGGGC}$ TTCTCCTGCTGACATCTGCCCTGGCCGGCCAGAGACAGGGGGACTCAGGCGGAATCCAACCTGAGTAGTAAATTCC AGTTTTCCAGCAACAAGGAACAGAACGGAGTACAAGATCCTCAGCATGAGAGAATTATTACTGTGTCTACTAATG GAAGTATTCACAGCCCAAGGTTTCCTCATACTTATCCAAGAAATACGGTCTTGGTATGGAGATTAGTAGCAGTAG AGGAAAATGTATGGATACAACTTACGTTTGATGAAAGATTTGGGCTTGAAGACCCAGAAGATGACATATGCAAGT ATGATTTTGTAGAAGTTGAGGAACCCAGTGATGGAACTATATTAGGGCGCTGGTGTGGTTCTGGTACTGTACCAG GAAAACAGATTTCTAAAGGAAATCAAATTAGGATAAGATTTGTATCTGATGAATATTTTCCTTCTGAACCAGGGT TCTGCATCCACTACAACATTGTCATGCCACAATTCACAGAAGCTGTGAGTCCTTCAGTGCTACCCCCTTCAGCTT TGCCACTGGACCTGCTTAATAATGCTATAACTGCCTTTAGTACCTTGGAAGACCTTATTCGATATCTTGAACCAG AGAGATGGCAGTTGGACTTAGAAGATCTATATAGGCCAACTTGGCAACTTCTTGGCAAGGCTTTTGTTTTTGGAA GAAAATCCAGAGTGGTGGATCTGAACCTTCTAACAGAGGAGGTAAGATTATACAGCTGCACACCTCGTAACTTCT CAGTGTCCATAAGGGAAGAACTAAAGAGAACCGATACCATTTTCTGGCCAGGTTGTCTCCTGGTTAAACGCTGTG ACCATGAGGAGTGTGACTGTGTGTGCAGAGGGAGCACAGGAGGAGCATCACCACCAGCAGCTCTTGCCCA GAGCTGTGCAGTGCAGTGGCTGATTCTATTAGAGAACGTATGCGTTATCTCCATCCTTAATCTCAGTTGTTTGCT TCAAGGACCTTTCATCTTCAGGATTTACAGTGCATTCTGAAAGAGGAGACATCAAACAGAATTAGGAGTTGTGCA TAAATAGATCACCAGCTAGTTTCAGAGTTACCATGTACGTATTCCACTAGCTGGGTTCTGTATTTCAGTTCTTTC GATACGGCTTAGGGTAATGTCAGTACAGGAAAAAAACTGTGCAAGTGAGCACCTGATTCCGTTGCCTTAAC ATGTAAACCAGAACATTCTATGTACTACAAACCTGGTTTTTAAAAAGGAACTATGTTGCTATGAATTAAACTTGT GTCATGCTGATAGGACAGGACTGGATTTTTCATATTTCTTATTAAAATTTCTGCCATTTAGAAGAAGAAGAACTACA TTCATGGTTTGGAAGAGATAAACCTGAAAAGAAGAGTGGCCTTATCTTCACTTTATCGATAAGTCAGTTTATTTG TTTCATTGTGTACATTTTTATATTCTCCTTTTGACATTATAACTGTTGGCTTTTCTAATCTTGTTAAATATCT ATTTTTACCAAAGGTATTTAATATTCTTTTTTATGACAACTTAGATCAACTATTTTTAGCTTGGTAAATTTTTTCT AAACACAATTGTTATAGCCAGAGGAACAAAGATGATATAAAATATTGTTGCTCTGACAAAAAATACATGTATTTCA TTCTCGTATGGTGCTAGAGTTAGATTAATCTGCATTTTAAAAAACTGAATTGGAATAGAATTGGTAAGTTGCAAA GACTTTTTGAAAATAATTAAATTATCATATCTTCCATTCCTGTTATTGGAGATGAAAATAAAAAGCAACTTATGA AAGTAGACATTCAGATCCAGCCATTACTAACCTATTCCTTTTTTGGGGAAATCTGAGCCTAGCTCAGAAAAACAT AAAGCACCTTGAAAAAGACTTGGCAGCTTCCTGATAAAGCGTGCTGTGCTGTGCAGTAGGAACACATCCTATTTA TTGTGATGTTGTGGTTTTATTATCTTAAACTCTGTTCCATACACTTGTATAAATACATGGATATTTTTATGTACA GAAGTATGTCTCTTAACCAGTTCACTTATTGTACTCTGGCAATTTAAAAGAAAATCAGTAAAATATTTTGCTTGT AAAATGCTTAATATNGTGCCTAGGTTATGTGGTGACTATTTGAATCAAAAATGTATTGAATCATCAAATAAAAGA

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FIGURE 286

MSLFGLLLTSALAGQRQGTQAESNLSSKFQFSSNKEQNGVQDPQHERIITVSTNGSIHSPRF
PHTYPRNTVLVWRLVAVEENVWIQLTFDERFGLEDPEDDICKYDFVEVEEPSDGTILGRWCGS
GTVPGKQISKGNQIRIRFVSDEYFPSEPGFCIHYNIVMPQFTEAVSPSVLPPSALPLDLLNNA
ITAFSTLEDLIRYLEPERWQLDLEDLYRPTWQLLGKAFVFGRKSRVVDLNLLTEEVRLYSCTP
RNFSVSIREELKRTDTIFWPGCLLVKRCGGNCACCLHNCNECQCVPSKVTKKYHEVLQLRPKT
GVRGLHKSLTDVALEHHEECDCVCRGSTGG

Important features:

signal sequence:

Amino acids 1-14

N-glycosylation sites:

Amino acids 25-29;55-59;254-258

N-myristoylation sites:

Amino acids 15-21;117-123;127-133;281-287;282-288;319-325

Amidation site:

Amino acids 229-233

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FIGURE 287

CAGCGCTGACTGCGCCGCGGAGAAAGCCAGTGGGAACCCAGACCCATAGGAGACCCGCGTCCC CGCTCGGCCTGGCCAGGCCCCGCGCTATGGAGTTCCTCTGGGCCCCTCTCTTGGGTCTGTGCT GCAGTCTGGCCGCTGATCGCCACACCGTCTTCTGGAACAGTTCAAATCCCAAGTTCCGGA ATGAGGACTACACCATACATGTGCAGCTGAATGACTACGTGGACATCATCTGTCCGCACTATG AAGATCACTCTGTGGCAGACGCTGCCATGGAGCAGTACATACTGTACCTGGTGGAGCATGAGG AGTACCAGCTGTGCCAGCCCCAGTCCAAGGACCAAGTCCGCTGGCAGTGCAACCGGCCCAGTG CCAAGCATGGCCCGGAGAAGCTGTCTGAGAAGTTCCAGCGCTTCACACCTTTCACCCTGGGCA AGGAGTTCAAAGAAGGACACAGCTACTACATCTCCAAACCCATCCACCAGCATGAAGACC ATCCACAGGAGAAGAGTTGCAGCAGATGACCCAGAGGTGCGGGTTCTACATAGCATCGGTC ACAGTGCTGCCCCACGCCTCTTCCCACTTGCCTGGACTGTGCTGCTCCTTCCACTTCTGCTGC TGCAAACCCCG**TGA**AGGTGTGTGCCACACCTGGCCTTAAAGAGGGACAGGCTGAAGAGAGGGA CAGGCACTCCAAACCTGTCTTGGGGCCACTTTCAGAGCCCCCAGCCCTGGGAACCACTCCCAC CACAGGCATAAGCTATCACCTAGCAGCCTCAAAACGGGTCAATATTAAGGTTTTCAACCGGAA GAGACAGTCCTTTCCCACCATTCCTGCCTTTAAGCCAAAGAAACAAGCTGTGCAGGCATGGTC CCTTAAGGCACAGTGGGAGCTGAGCTGGAAGGGGCCACGTGGATGGGCAAAGCTTGTCAAAGA TTTCTTGCTTGGAAGCCAGGTACAGGAGGGCAGCATGCTTGGGCTGACCCAGCATCTCCCAG CAAGACCTCATCTGTGGAGCTGCCACAGAGAAGTTTGTAGCCAGGTACTGCATTCTCTCCCAT CCTGGGGCAGCACTCCCCAGAGCTGTGCCAGCAGGGGGGGCTGTGCCAACCTGTTCTTAGAGTG TAGCTGTAAGGGCAGTGCCCATGTGTACATTCTGCCTAGAGTGTAGCCTAAAGGGCAGGGCCC TTTATACAATGTTCTTTGTCTCAAAATAAAGCAATGTGTTTTTTCGG

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FIGURE 288

MEFLWAPLIGLCCSLAAADRHTVFWNSSNPKFRNEDYTIHVQLNDYVDIICPHYEDHSADAAM EQYILYLVEHEEYQLCQPQSKDQVRWQCNRPSAKHGPEKLSEKFQRFTPFTLGKEFKEGHSYY YISKPIHQHEDRCLRLKVTVSGKITHSPQAHDNPQEKRLAADDPEVRVLHSIGHSAAPRLFPL AWTVLLLPLLLLQTP

Important features:

Signal sequence:

Amino acids 1-17

N-glycosylation site:

Amino acids 26-30

Tyrosine kinase phosphorylation site:

Amino acids 118-127

N-myristoylation site:

Amino acids 10-16

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FIGURE 289

CGGACGCGTGGGCGGACGCGTGGGCGGCCCACGCGCGCGGGCTGGGGCGGTCGCTTCTTC CTTCTCCGTGGCCTACGAGGGTCCCCAGCCTGGGTAAAGATGGCCCCATGGCCCCCGAAGGGC CTAGTCCCAGCTGTGCTCTGGGGCCTCAGCCTCTTCCTCAACCTCCCAGGACCTATCTGGCTC CAGCCCTCTCCACCTCCCCAGTCTTCTCCCCCGCCTCAGCCCCATCCGTGTCATACCTGCCGG GGACTGGTTGACAGCTTTAACAAGGGCCTGGAGAGAACCATCCGGGACAACTTTGGAGGTGGA AACACTGCCTGGGAGGAAGAGATTTGTCCAAATACAAAGACAGTGAGACCCGCCTGGTAGAG GAGCTGGTGGAGAGCTGGTTGTCACAAGCAGCAGGAGGCCCCGGACCTCTTCCAGTGGCTG TGCTCAGATTCCCTGAAGCTCTGCTGCCCCGCAGGCACCTTCGGGCCCTCCTGCCTTCCCTGT CCTGGGGGAACAGAGGCCCTGCGGTGGCTACGGGCAGTGTGAAGGAAAGGGACACGAGGG GGCAGCGGCACTGTGACTGCCAAGCCGGCTACGGGGGTGAGGCCTGTGGCCAGTGTGGCCTT GGCTACTTTGAGGCAGAACGCAACGCCAGCCATCTGGTATGTTCGGCTTGTTTTGGCCCCTGT GCCCGATGCTCAGGACCTGAGGAATCAAACTGTTTGCAATGCAAGAAGGGCTGGGCCCTGCAT CACCTCAAGTGTGTAGACATTGATGAGTGTGGCACAGAGGGAGCCAACTGTGGAGCTGACCAA ATGGGGGCAGGCCAGGTCGCTGTAAGAAGTGTAGCCCTGGCTATCAGCAGGTGGGCTCCAAG TGTCTCGATGTGGATGAGTGTGAGACAGAGGTGTGTCCGGGAGAGAACAAGCAGTGTGAAAAC ACCGAGGGCGGTTATCGCTGCATCTGTGCCGAGGGCTACAAGCAGATGGAAGGCATCTGTGTG AAGGAGCAGATCCCAGAGTCAGCAGGCTTCTTCTCAGAGATGACAGAAGACGAGTTGGTGGTG CTGCAGCAGATGTTCTTTGGCATCATCTGTGCACTGGCCACGCTGGCTAAGGGCGAC TTGGTGTTCACCGCCATCTTCATTGGGGCTGTGGCGGCCATGACTGGCTACTGGTTGTCAGAG CGCAGTGACCGTGTGCTGGAGGGCTTCATCAAGGGCAGA**TAA**TCGCGGCCACCACCTGTAGGA CCTCCTCCCACCCACGCTGCCCCCAGAGCTTGGGCTGCCCTCCTGCTGGACACTCAGGACAGC TTGGTTTATTTTTGAGAGTGGGGTAAGCACCCCTACCTGCCTTACAGAGCAGCCCAGGTACCC AGGCCCGGGCAGACAAGGCCCCTGGGGTAAAAAGTAGCCCTGAAGGTGGATACCATGAGCTCT TCACCTGGCGGGACTGCCAGGCTTCACAATGTGTGAATTTCAAAAGTTTTTCCTTAATGGTG GCTGCTAGAGCTTTGGCCCCTGCTTAGGATTAGGTGGTCCTCACAGGGGTGGGGCCCATCACAG CTCCCTCCTGCCAGCTGCATGCTGCCAGTTCCTGTTCTGTTTCACCACATCCCCACACCCCA AAAAAAAAA

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FIGURE 290

MAPWPPKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERT IRDNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQE APDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGG EACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTE GANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCP GENKQCENTEGGYRCICAEGYKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFFGIIICAL ATLAAKGDLVFTAIFIGAVAAMTGYWLSERSDRVLEGFIKGR

Important features:

Signal sequence:

Amino acids 1-29

Transmembrane domain:

Amino acids 342-392

N-glycosylation sites:

Amino acids 79-83;205-209

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 290-294

Aspartic acid and asparagine hydroxylation site:

Amino acids 321-333

EGF-like domain cysteine pattern signature:

Amino acids 181-193

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FIGURE 291

CAGGTCCAACTGCACCTCGGTTCTATCGATTGAATTCCCCGGGGGATCCTCTAGAGATCCCTCGACCTCGACCCAC ACATCGAAGGTGGGGTGGGACCAGGCTGCCCCTCGCCCCAGCATCCAAGTCCTCCCTTGGGCGCCCGTGGCCCTG CAGACTCTCAGGGCTAAGGTCCTCTGTTGCTTTTTTGGTTCCACCTTAGAAGAGGCTCCGCTTGACTAAGAGTAGC TTGAAGGAGGCACCATGCAGGAGCTGCATCTGCTCTGGTGGGCCCTTCTCCTGGGCCTGGCCTAGGCCTGCCCTG AGCCCTGCGACTGTGGGGAAAAGTATGGCTTCCAGATCGCCGACTGTGCCTACCGCGACCTAGAATCCGTGCCGC CTGGCTTCCCGGCCAATGTGACTACACTGAGCCTGTCAGCCAACCGGCTGCCAGGCTTGCCGGAGGGTGCCTTCA GGGAGGTGCCCTGCTGCAGTCGCTGTGGCTGGCACACAATGAGATCCGCACGGTGGCCGCCGGAGCCCTGGCCT CTCTGAGCCATCTCAAGAGCCTGGACCTCAGCCACAATCTCATCTCTGACTTTGCCTGGAGCGACCTGCACAACC TCAGTGCCCTCCAATTGCTCAAGATGGACAGCAACGAGCTGACCTTCATCCCCCGCGACGCCTTCCGCAGCCTCC GTGCTCTGCGCTCGCTGCAACTCAACCACCGCTTGCACACTTGGCCGAGGGCACCTTCACCCCGCTCACCG $\tt CGCTGTCCCACCTGCAGATCAACGAGAACCCCTTCGACTGCACCTGCGGCATCGTGTGGCTCAAGACATGGGCCC$ TGACCACGCCGTGTCCATCCCGGAGCAGGACAACATCGCCTGCACCTCACCCCATGTGCTCAAGGGTACACCGC CTGTGGCCAGCTCCCAGCCGCCTTCCAGGCCTTTGCCAATGGCAGCCTGCTTATCCCCGACTTTGGCAAGCTGG AGGAAGGCACCTACAGCTGCCTGGCCACCAATGAGCTGGGCAGTGCTGAGAGGCTCAGTGGACGTGGCACTGGCCA CGCCCGGTGAGGGTGAGGACACACTGGGGCGCAGGTTCCATGGCAAAGCGGTTGAGGGAAAGGGCTGCTATA CGGTTGACAACGAGGTGCAGCCATCAGGGCCGGAGGACAATGTGGTCATCATCTACCTCAGCCGTGCTGGGAACC CTGAGGCTGCAGTCGCAGAAGGGGTCCCTGGGCAGCTGCCCCCAGGCCTGCTCCTGCTGGGCCAAAGCCTCCTCC TTTAAGTGCTGCAGGGGTCTGGGGTTGGCAACTCCTGAGGCCTGCATGGGTGACTTCACATTTTCCTACCTCTCC TTCTAATCTCTTCTAGAGCACCTGCTATCCCCAACTTCTAGACCTGCTCCAAACTAGTGACTAGGATAGAATTTG ATCCCCTAACTCACTGTCTGCGGTGCTCATTGCTGCTAACAGCATTGCCTGTGCTCTCCTCTCAGGGGCAGCATG CTAACGGGGCGACGTCCTAATCCAACTGGGAGAAGCCTCAGTGGTGGAATTCCAGGCACTGTGACTGTCAAGCTG GCAAGGGCCAGGATTGGGGGAATGGAGCTGGGGCTTAGCTGGGAGGTGGTCTGAAGCAGACAGGGAATGGGAGAG GAGGATGGGAAGTAGACAGTGGCTGGTATGGCTCTGAGGCTCCCTGGGGCCTGCTCAAGCTCCTCCTGCTCCTTG CTGTTTTCTGATGATTTTGGGGGGCTTGGGAGTCCCTTTGTCCTCATCTGAGACTGAAATGTGGGGATCCAGGATGG $\tt CCTTCCTTCCTCCTCCTCCTCCTCAGCCTGCAACCTCTATCCTGGAACCTGTCCTCCCTTTCTCCCCAACT$ ATGCATCTGTTGTCTCCTCTCCAAAGGCCAGCCAGCTTGGGAGCAGCAGAGAAATAAACAGCATTTCTGATG CCAAAAAAAAAAAAAAAAAGGGCGGCCGCGACTCTAGAGTCGACCT

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FIGURE 292

MQELHLLWWALLLGLAQACPEPCDCGEKYGFQIADCAYRDLESVPPGFPANVTTLSLSANRLP
GLPEGAFREVPLLQSLWLAHNEIRTVAAGALASLSHLKSLDLSHNLISDFAWSDLHNLSALQL
LKMDSNELTFIPRDAFRSLRALRSLQLNHNRLHTLAEGTFTPLTALSHLQINENPFDCTCGIV
WLKTWALTTAVSIPEQDNIACTSPHVLKGTPLSRLPPLPCSAPSVQLSYQPSQDGAELRPGFV
LALHCDVDGQPAPQLHWHIQIPSGIVEITSPNVGTDGRALPGTPVASSQPRFQAFANGSLLIP
DFGKLEEGTYSCLATNELGSAESSVDVALATPGEGGEDTLGRRFHGKAVEGKGCYTVDNEVQP
SGPEDNVVIIYLSRAGNPEAAVAEGVPGQLPPGLLLLGQSLLLFFFLTSF

Important features:

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 403-418

N-glycosylation sites:

Amino acids 51-55,120-124,309-313

Tyrosine kinase phosphorylation site:

amino acids 319-326

N-myristoylation sites:

amino acids 14-20,64-70,92-98,218-224,294-300,323-329,334-340,350-356,394-400

Amidation site:

amino acids 355-359

Leucine Rich Repeat:

amino acids 51-74,75-98, 99-122,123-146,147-170

Leucine rich repeat C-terminal domain:

amino acids 180-230

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FIGURE 293

ACTTGGAGCAAGCGGCGGCGGGGGAGACAGAGGCAGAGGCAGAAGCTGGGGCTCCGTCCTCGCCTCCCACGAGCG ATCCCCGAGGAGAGCCGCCCTCGGCGAGGCGAAGAGGCCGACGAGGAAGACCCGGGTGGCTGCCCCTGCC TCGCTTCCCAGGCGCCGGCGGCTGCAGCCTTGCCCCTCTTGCTCGCCTTGAAAATGGAAAAGATGCTCGCAGGCT GCTTTCTGCTGATCCTCGGACAGATCGTCCTCCTCCCTGCCGAGGCCAGGGAGCCGTCACGTGGGAGGTCCATCT CTAGGGGCAGACACGCTCGGACCCACCCGCAGACGGCCCTTCTGGAGAGTTCCTGTGAGAACAAGCGGGCAGACC TGGTTTTCATCATTGACAGCTCTCGCAGTGTCAACACCCATGACTATGCAAAGGTCAAGGAGTTCATCGTGGACA TCTTGCAATTCTTGGACATTGGTCCTGATGTCACCCGAGTGGGCCTGCTCCAATATGGCAGCACTGTCAAGAATG AGTTCTCCCTCAAGACCTTCAAGAGGAAGTCCGAGGTGGAGCGTGCTGTCAAGAGGATGCGGCATCTGTCCACGG GCACCATGACTGGGCTGGCCATCCAGTATGCCCTGAACATCGCATTCTCAGAAGCAGAGGGGGCCCGGCCCCTGA GGGAGAATGTGCCACGGGTCATAATGATCGTGACAGATGGGAGACCTCAGGACTCCGTGGCCGAGGTGGCTGCTA GGAGTGAGCCCCATGAGGACCATGTCTTCCTTGTGGCCAATTTCAGCCAGATTGAGACGCTGACCTCCGTGTTCC AGAAGAAGTTGTGCACGGCCCACATGTGCAGCACCCTGGAGCATAACTGTGCCCACTTCTGCATCAACATCCCTG GCTCATACGTCTGCAGGTGCAAACAAGGCTACATTCTCAACTCGGATCAGACGTCGCAGAATCCAGGATCTGT GTGCCATGGAGGACCACAACTGTGAGCAGCTCTGTGTGAATGTGCCGGGCTCCTTCGTCTGCCAGTGCTACAGTG GCTACGCCCTGGCTGAGGATGGGAAGAGGTGTGTGGCTGTGGACTACTGTGCCTCAGAAAACCACGGATGTGAAC ATGAGTGTGTAAATGCTGATGGCTCCTACCTTTGCCAGTGCCATGAAGGATTTGCTCTTAACCCAGATGAAAAAA CGTGCACAAGGATCAACTACTGTGCACTGAACAAACCGGGCTGTGAGCATGAGTGCGTCAACATGGAGGAGAGCT AGCAGGACCATGGCTGTGAGCAGCTGTGTCTGAACACGGAGGATTCCTTCGTCTGCCAGTGCTCAGAAGGCTTCC GTGTCAACATGGACAGATCCTTTGCCTGTCAGTGTCCTGAGGGACACGTGCTCCGCAGCGATGGGAAGACGTGTG GCCAGTGCTTTGAAGGTTATATACTCCGTGAAGATGGAAAAACCTGCAGAAGGAAAGATGTCTGCCAAGCTATAG ACCATGGCTGTGAACACATTTGTGTGAACAGTGACGACTCATACACGTGCGAGTGCTTGGAGGGATTCCGGCTCG $\tt CTGAGGATGGGAAACGCTGCCGAAGGAAGGATGTCTGCAAATCAACCCACCATGGCTGCGAACACATTTGTGTTA$ ATAATGGGAATTCCTACATCTGCAAATGCTCAGAGGGATTTGTTCTAGCTGAGGACGGAAGACGGTGCAAGAAAT GCACTGAAGGCCCAATTGACCTGGTCTTTGTGATCGATGGATCCAAGAGTCTTGGAGAAGAGAATTTTGAGGTCG TGAAGCAGTTTGTCACTGGAATTATAGATTCCTTGACAATTTCCCCCAAAGCCGCTCGAGTGGGGCTGCTCCAGT ATTCCACACAGGTCCACACAGAGTTCACTCTGAGAAACTTCAACTCAGCCAAAGACATGAAAAAAAGCCGTGGCCC ACATGAAATACATGGGAAAGGGCTCTATGACTGGGCTGGCCCTGAAACACATGTTTGAGAGAAGTTTTACCCAAG ATGAGATAAGTGAAAAACTCAAGAAAGGCATCTGTGAAGCTCTAGAAGACTCCGATGGAAGACAGGACTCTCCAG CAGGGGAACTGCCAAAAACGGTCCAACAGCCAACAGAATCTGAGCCAGTCACCATAAATATCCAAGACCTACTTT CCTGTTCTAATTTTGCAGTGCAACACAGATATCTGTTTGAAGAAGACAATCTTTTACGGTCTACACAAAAGCTTT CCCATTCAACAAAACCTTCAGGAAGCCCTTTGGAAGAAAAACACGATCAATGCAAATGTGAAAACCTTATAATGT TCCAGAACCTTGCAAACGAAGAAGTAAGAAATTAACACAGCGCTTAGAAGAAATGACACAGAGAATGGAAGCCC TGGAAAATCGCCTGAGATACAGA<u>TGA</u>AGATTAGAAATCGCGACACATTTGTAGTCATTGTATCACGGATTACAAT GAACGCAGTGCAGAGCCCCAAAGCTCAGGCTATTGTTAAATCAATAATGTTGTGAAGTAAAACAATCAGTACTGA GAAACCTGGTTTGCCACAGAACAAGACAAGAAGTATACACTAACTTGTATAAATTTATCTAGGAAAAAAATCCT TCAGAATTCTAAGATGAATTTACCAGGTGAGAATGAATAAGCTATGCAAGGTATTTTGTAATATACTGTGGACAC AACTTGCTTCTGCCTCATCCTGCCTTAGTGTGCAATCTCATTTGACTATACGATAAAGTTTGCACAGTCTTACTT CTGTAGAACACTGGCCATAGGAAATGCTGTTTTTTTGTACTGGACTTTACCTTGATATATGTATATGGATGTATG CATAAAATCATAGGACATATGTACTTGTGGAACAAGTTGGATTTTTTATACAATATTAAAATTCACCACTTCAG

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FIGURE 294

MEKMLAGCFLLILGQIVLLPAEARERSRGRSISRGRHARTHPQTALLESSCENKRADLVFIID SSRSVNTHDYAKVKEFIVDILQFLDIGPDVTRVGLLQYGSTVKNEFSLKTFKRKSEVERAVKR MRHLSTGTMTGLAIQYALNIAFSEAEGARPLRENVPRVIMIVTDGRPQDSVAEVAAKARDTGI LIFAIGVGQVDFNTLKSIGSEPHEDHVFLVANFSQIETLTSVFQKKLCTAHMCSTLEHNCAHF CINIPGSYVCRCKQGYILNSDQTTCRIQDLCAMEDHNCEQLCVNVPGSFVCQCYSGYALAEDG KRCVAVDYCASENHGCEHECVNADGSYLCQCHEGFALNPDEKTCTRINYCALNKPGCEHECVN MEESYYCRCHRGYTLDPNGKTCSRVDHCAQQDHGCEQLCLNTEDSFVCQCSEGFLINEDLKTC SRVDYCLLSDHGCEYSCVNMDRSFACQCPEGHVLRSDGKTCAKLDSCALGDHGCEHSCVSSED SFVCQCFEGYILREDGKTCRRKDVCQAIDHGCEHICVNSDDSYTCECLEGFRLAEDGKRCRRK DVCKSTHHGCEHICVNNGNSYICKCSEGFVLAEDGRRCKKCTEGPIDLVFVIDGSKSLGEENF EVVKQFVTGIIDSLTISPKAARVGLLQYSTQVHTEFTLRNFNSAKDMKKAVAHMKYMGKGSMT GLALKHMFERSFTQGEGARPLSTRVPRAAIVFTDGRAQDDVSEWASKAKANGITMYAVGVGKA IEEELQEIASEPTNKHLFYAEDFSTMDEISEKLKKGICEALEDSDGRQDSPAGELPKTVQQPT ESEPVTINIQDLLSCSNFAVQHRYLFEEDNLLRSTQKLSHSTKPSGSPLEEKHDQCKCENLIM FQNLANEEVRKLTQRLEEMTQRMEALENRLRYR

Important features:

Signal sequence:

Amino acids 1-23

N-glycosylation site:

Amino acids 221-225

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 115-119;606-610;892-896

N-myristoylation sites:

Amino acids 133-139;258-264;299-305;340-346;453-459;494-500;639-645;690-694;752-758;792-798

Amidation sites:

Amino acids 314-318;560-564;601-605

Aspartic acid and asparagine hydroxylation sites:

Amino acids 253-265;294-306;335-347;376-388;417-429;458-470;540-552;581-593

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FIGURE 295

GGCCGGAGCACGCCGCAGGACCTGGAGCTCCGGCTGCGTCTTCCCGCAGCGCTACCCGC GCCGGAGGCCGCCAAGAAGCCGACGCCCTGCCACCGGTGCCGGGGGCTGGTGGACAAGTTTAA CCAGGGGATGGTGGACACCGCAAAGAAGAACTTTGGCGGCGGGAACACGGCTTGGGAGGAAAA GACGCTGTCCAAGTACGAGTCCAGCGAGATTCGCCTGCTGGAGATCCTGGAGGGGGCTGTGCGA GAGCAGCGACTTCGAATGCAATCAGATGCTAGAGGCGCAGGAGGAGCACCTGGAGGCCTGGTG GCTGCAGCTGAAGAGCGAATATCCTGACTTATTCGAGTGGTTTTTGTGTGAAGACACTGAAAGT GTGCTGCTCCAGGAACCTACGGTCCCGACTGTCTCGCATGCCAGGGCGGATCCCAGAGGCC CTGCAGCGGGAATGGCCACTGCAGCGGAGATGGGAGCAGACAGGGCGACGGGTCCTGCCGGTG GAACGAGACCCACAGCATCTGCACAGCCTGTGACGAGTCCTGCAAGACGTGCTCGGGCCTGAC ${\tt CAACAGAGACTGCGGCGAGTGTGAAGTGGGCTGGGTGCTGGACGAGGGCGCCTGTGTGGATGT}$ GGACGAGTGTGCGGCCGAGCCGCCTCCCTGCAGCGCTGCGCAGTTCTGTAAGAACGCCAACGG CTCCTACACGTGCGAAGAGTGTGACTCCAGCTGTGTGGGCTGCACAGGGGAAGGCCCAGGAAA CTGTAAAGAGTGTATCTCTGGCTACGCGAGGGAGCACGGACAGTGTGCAGATGTGGACGAGTG CTCACTAGCAGAAAAACCTGTGTGAGGAAAAACGAAAACTGCTACAATACTCCAGGGAGCTA CGTCTGTGTGTGTCCTGACGGCTTCGAAGAAACGGAAGATGCCTGTGTGCCGCCGGCAGAGGC TGAAGCCACAGAAGGAGAAAGCCCGACACAGCTGCCCTCCCGCGAAGACCTG**TAA**TGTGCCGG ACTTACCCTTTAAATTATTCAGAAGGATGTCCCGTGGAAAATGTGGCCCTGAGGATGCCGTCT CCTGCAGTGGACAGCGGGGGGAGAGGCTGCCTGCTCTCTAACGGTTGATTCTCATTTGTCCC TTAAACAGCTGCATTTCTTGGTTGTTCTTAAACAGACTTGTATATTTTGATACAGTTCTTTGT

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FIGURE 296

MRLPRRAALGLLPLLLLPPAPEAAKKPTPCHRCRGLVDKFNQGMVDTAKKNFGGGNTAWEEK
TLSKYESSEIRLLEILEGLCESSDFECNQMLEAQEEHLEAWWLQLKSEYPDLFEWFCVKTLKV
CCSPGTYGPDCLACQGGSQRPCSGNGHCSGDGSRQGDGSCRCHMGYQGPLCTDCMDGYFSSLR
NETHSICTACDESCKTCSGLTNRDCGECEVGWVLDEGACVDVDECAAEPPPCSAAQFCKNANG
SYTCEECDSSCVGCTGEGPGNCKECISGYAREHGQCADVDECSLAEKTCVRKNENCYNTPGSY
VCVCPDGFEETEDACVPPAEAEATEGESPTOLPSREDL

Important features:

Signal peptide:

Amino acids 1-24

N-glycosylation sites:

Amino acids 190-194;251-255

Glycosaminoglycan attachment sites:

Amino acids 149-153;155-159

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 26-30

Tyrosine kinase phosphorylation site:

Amino acids 303-310

N-myristoylation sites:

Amino acids 44-50;54-60;55-61;81-87;150-156;158-164;164-170; 252-258;313-319

Aspartic acid and asparagine hydroxylation site:

Amino acids 308-320

EGF-like domain cysteine pattern signature:

Amino acids 166-178

Leucine zipper pattern:

Amino acids 94-116

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FIGURE 297

ATGTTGGGCAACATTTATTTAACATGCTCCACAGCCCGGACCCTGGCATCATGCTGCTATTCCTGCAAATACTGA CACCTTCAAAAAGTACATCAATATTATATCATTAAGGAAATAGTAACCTTCTCTTCTCCAATATGCATGACATTT TTGGACAATGCAATTGTGGCACTGGCACTTATTTCAGTGAAGAAAAACTTTGTGGTTCTATGGCATTCATCATTT CCATTACATTTCTGAAGAAGAAAGCTAAGATGAAGGACATGCCACTCCGAATTCATGTGCTACTTGGCCTAGCTA TCACTACACTAGTACAAGCTGTAGATAAAAAAGTGGATTGTCCACGGTTATGTACGTGTGAAATCAGGCCTTGGT TTACACCCAGATCCATTTATATGGAAGCATCTACAGTGGATTGTAATGATTTAGGTCTTTTAACTTTCCCAGCCA GATTGCCAGCTAACACACAGATTCTTCTCCTACAGACTAACAATATTGCAAAAATTGAATACTCCACAGACTTTC CAGTAAACCTTACTGGCCTGGATTTATCTCAAAACAATTTATCTTCAGTCACCAATATTAATGTAAAAAAGATGC ACTTACAAGAACTCTATATTAATCACAACTTGCTTTCTACAATTTCACCTGGAGCCTTTATTGGCCTACATAATC TTCTTCGACTTCATCTCAATTCAAATAGATTGCAGATGATCAACAGTAAGTGGTTTGATGCTCTTCCAAATCTAG AGATTCTGATGATTGGGGAAAATCCAATTATCAGAATCAAAGACATGAACTTTAAGCCTCTTATCAATCTTCGCA TCTCTTTTTACGATAACAGGCTTATTAAAGTACCCCATGTTGCTCTTCAAAAAGTTGTAAATCTCAAATTTTTGG ATCTAAATAAAATCCTATTAATAGAATACGAAGGGGTGATTTTAGCAATATGCTACACTTAAAAGAGTTGGGGA TAAATAATATGCCTGAGCTGATTTCCATCGATAGTCTTGCTGTGGATAACCTGCCAGATTTAAGAAAAATAGAAG CTACTAACAACCCTAGATTGTCTTACATTCACCCCAATGCATTTTTCAGACTCCCCAAGCTGGAATCACTCATGC TGAACAGCAATGCTCTCAGTGCCCTGTACCATGGTACCATTGAGTCTCTGCCAAACCTCAAGGAAATCAGCATAC ACAGTAACCCCATCAGGTGTGACTGTCATCCGTTGGATGAACATGAACAAAACCAACATTCGATTCATGGAGC CAGATTCACTGTTTTGCGTGGACCCACCTGAATTCCAAGGTCAGAATGTTCGGCAAGTGCATTTCAGGGACATGA TGGAAATTTGTCTCCCTCTTATAGCTCCTGAGAGCTTTCCTTCTAATCTAAATGTAGAAGCTGGGAGCTATGTTT CCTTTCACTGTAGAGCTACTGCAGAACCACAGCCTGAAATCTACTGGATAACACCTTCTGGTCAAAAACTCTTGC CTAATACCCTGACAGACAAGTTCTATGTCCATTCTGAGGGAACACTAGATATAAATGGCGTAACTCCCAAAGAAG CTTTTCCACAGATAACAATGGCTCTTTGAATATTAAAATAAGAGATATTCAGGCCAATTCAGTTTTGGTGTCCT GGAAAGCAAGTTCTAAAATTCTCAAATCTAGTGTTAAATGGACAGCCTTTGTCAAGACTGAAAATTCTCATGCTG CGCAAAGTGCTCGAATACCATCTGATGTCAAGGTATATAATCTTACTCATCTGAATCCATCAACTGAGTATAAAA TTTGTATTGATATTCCCACCATCTATCAGAAAAACAGAAAAAATGTGTAAATGTCACCACCAAAGGTTTGCACC CTGATCAAAAAGAGTATGAAAAGAATAATACCACAACACTTATGGCCTGTCTTGGAGGCCTTCTGGGGGATTATTG GTGTGATATGTCTTATCAGCTGCCTCTCTCCAGAAATGAACTGTGATGGTGGACACAGCTATGTGAGGAATTACT TACAGAAACCAACCTTTGCATTAGGTGAGCTTTATCCTCCTCTGATAAATCTCTGGGAAGCAGGAAAAGAAAAAA GTACATCACTGAAAGTAAAAGCAACTGTTATAGGTTTACCAACAAATATGTCCTAAAAAACCACCAAGGAAACCTA CTCCAAAAATGAAC

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FIGURE 298

MKDMPLRIHVLLGLAITTLVQAVDKKVDCPRLCTCEIRPWFTPRSIYMEASTVDCNDLGLLTF
PARLPANTQILLLQTNNIAKIEYSTDFPVNLTGLDLSQNNLSSVTNINVKKMPQLLSVYLEEN
KLTELPEKCLSELSNLQELYINHNLLSTISPGAFIGLHNLLRLHLNSNRLQMINSKWFDALPN
LEILMIGENPIIRIKDMNFKPLINLRSLVIAGINLTEIPDNALVGLENLESISFYDNRLIKVP
HVALQKVVNLKFLDLNKNPINRIRRGDFSNMLHLKELGINNMPELISIDSLAVDNLPDLRKIE
ATNNPRLSYIHPNAFFRLPKLESLMLNSNALSALYHGTIESLPNLKEISIHSNPIRCDCVIRW
MNMNKTNIRFMEPDSLFCVDPPEFQGQNVRQVHFRDMMEICLPLIAPESFPSNLNVEAGSYVS
FHCRATAEPQPEIYWITPSGQKLLPNTLTDKFYVHSEGTLDINGVTPKEGGLYTCIATNLVGA
DLKSVMIKVDGSFPQDNNGSLNIKIRDIQANSVLVSWKASSKILKSSVKWTAFVKTENSHAAQ
SARIPSDVKVYNLTHLNPSTEYKICIDIPTIYQKNRKKCVNVTTKGLHPDQKEYEKNNTTTLM
ACLGGLLGIIGVICLISCLSPEMNCDGGHSYVRNYLQKPTFALGELYPPLINLWEAGKEKSTS
LKVKATVIGLPTNMS

Important features:

Signal sequence:

amino acids 1-22

Transmembrane domain:

amino acids 633-650

N-glycosylation site.

amino acids 93-97, 103-107, 223-227, 382-386, 522-526, 579-583, 608-612, 624-628, 625-629

Casein kinase II phosphorylation site.

amino acids 51-55, 95-99, 242-246, 468-472, 487-491

Tyrosine kinase phosphorylation site.

amino acids 570-579

N-myristoylation site.

amino acids 13-19, 96-102, 158-164, 221-227, 352-358, 437-443, 491-497, 492-498, 634-640, 702-708

Cell attachment sequence.

amino acids 277-280

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FIGURE 299

GCTGTGGGAACCTCTCCACGCGCACGAACTCAGCCAACGATTTCTGATAGATTTTTGGGAGGTT TGACCAGAGATGCAAGGGGTGAAGGAGCGCTTCCTACCGTTAGGGAACTCTGGGGACAGAGCG CCCCGGCCGCCTGATGGCCGAGCCAGGGTGCGACCCAGGACCGAGGCGTCGGGAACCAT ACCATGCCCGGATCCCCAAGACCCTAAAGTTCGTCGTCGTCATCGTCGCGGTCCTGCCCA GTCCTAGCTTACTCTGCCACCACTGCCCGGCAGGAGGAAGTTCCCCAGCAGACAGTGGCCCCA CAGCAACAGAGGCACAGCTTCAAGGGGGAGGAGTGTCCAGCAGGATCTCATAGATCAGAACAT ACTGGAGCCTGTAACCCGTGCACAGAGGGTGTGGATTACACCAACGCTTCCAACAATGAACCT TCTTGCTTCCCATGTACAGTTTGTAAATCAGATCAAAAACATAAAAGTTCCTGCACCATGACC AGAGACACAGTGTGTCAGTGTAAAGAAGGCACCTTCCGGAATGAAAACTCCCCAGAGATGTGC CGGAAGTGTAGCAGGTGCCCTAGTGGGGAAGTCCAAGTCAGTAATTGTACGTCCTGGGATGAT ATCCAGTGTGTTGAAGAATTTGGTGCCAATGCCACTGTGGAAACCCCAGCTGCTGAAGAGACA ATGAACACCAGCCCGGGGACTCCTGCCCCAGCTGCTGAAGAGACAATGAACACCAGCCCAGGG ACTCCTGCCCCAGCTGCTGAAGAGACAATGACCACCAGCCCGGGGACTCCTGCCCCAGCTGCT GAAGAGACAATGACCACCCGGGGACTCCTGCCCCAGCTGCTGAAGAGACAATGACCACC AGCCCGGGGACTCCTGCCTCTTCTCATTACCTCTCATGCACCATCGTAGGGATCATAGTTCTA AAAGGTTCAGGTAGGCGCTGAGGGGGGGGGGGGGGCGCTGGACACTCTCTGCCCTGCCTCCCT CTGCTGTTCCCACAGACAGAAACGCCTGC

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FIGURE 300

MARIPKTLKFVVVIVAVLLPVLAYSATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRSEHT GACNPCTEGVDYTNASNNEPSCFPCTVCKSDQKHKSSCTMTRDTVCQCKEGTFRNENSPEMCR KCSRCPSGEVQVSNCTSWDDIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGT PAPAAEETMTTSPGTPAPAAEETMTTSPGTPAPAAEETMTTSPGTPASSHYLSCTIVGIIVLI VLLIVFV

Important features:

Signal peptide:

Amino acids 1-29

Transmembrane domain:

Amino acids 240-259

N-glycosylation site:

Amino acids 77-81;140-144;156-160

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 126-130

N-myristoylation sites:

Amino acids 56-62;72-78;114-120;154-160;233-239

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FIGURE 301

CACAAGCATCTTAATTTGAATCCACAAAGTTTCATGTAATGAAAAGAAATACATAATTTTAAT TCAACCCGAGTGTTTTCCAAGAAGATTGTATTTGCTTAAATTGCTACAGTAATTCAAGAGACA GCCCTGTCTGGACACAGAGTTACTGTGGATTTTTAAGAGACTCAGTTAAAGAATTTAGGAATT TCTGATTCATTTAAAGGATTTACAAATTCATCAACCCCTGAAAACTAAAGCAAATTGAACAGG AAAAAAAAAAAAGAAG**ATG**GGTTTTTTAAGTCCAATATATGTTATTTTCTTCTTTTTTTGGAGTC AAAGTACATTGCCAATATGAAACTTATCAGTGGGATGAAGACTATGACCAAGAGCCAGATGAT GATTACCAAACAGGATTCCCATTTCGTCAAAATGTAGACTACGGAGTTCCTTTTCATCAGTAT AATCGCAAACTCAAGACTATCCCAAATATTCCGATGCACATTCAGCAACTCTACCTTCAGTTC AATGAAATTGAGGCTGTGACTGCAAATTCATTCATCAATGCAACTCATCTTAAAGAAATTAAC CTCAGCCACAACAAATTAAATCTCAAAAGATTGATTATGGTGTGTTTTGCTAAGCTTCCAAAT CTACTACAACTTCATCTAGAGCATAATAATTTAGAAGAATTTCCATTTCCTCTTCCTAAATCT CTAGTAAACTTGACCATGCTTGATCTCTGTTATAATTATCTTCATGATTCTCTGCTAAAAGAC AAAATCTTTGCCAAAATGGAAAAACTAATGCAGCTCAACCTCTGCAGTAACAGATTAGAATCA ATGCCTCCTGGTTTGCCTTCTTCACTTATGTATCTGTCTTTAGAAAATAATTCAATTTCTTCT ATACCCGAAAATACTTCGACAAACTTCCAAAACTTCATACTCTAAGAATGTCACACAACAAA CTACAAGACATCCCATATAATATTTTTAATCTTCCCAACATTGTAGAACTCAGTGTTGGACAC AACAAATTGAAGCAAGCATTCTATATTCCAAGAAATTTGGAACACCTATACCTACAAAATAAT GAAATAGAAAAGATGAATCTTACAGTGATGTCCTTCTATTGACCCACTACATTACCACCAT TTAACATACATTCGTGTGGACCAAAATAAACTAAAAGAACCAATAAGCTCATACATCTTCTTC TGCTTCCCTCATATACACACTATTTATTATGGTGAACAACGAAGCACTAATGGTCAAACAATA CAACTAAAGACACAAGTTTTCAGGAGATTTCCAGATGATGATGATGAAAGTGAAGATCACGAT GATCCTGACAATGCTCATGAGAGCCCAGAACAAGAAGGAGCAGAAGGGCACTTTGACCTTCAT TATTATGAAAATCAAGAA**TAG**CAAGAAACTATATAGGTATACACTTACGACTTCACAAAACCTA TACTTAATATAGTAAATCTAAGTAAACATGTATTACTCAAAGTAATATATTTAGAATTATGTA TTAGTATAAGATCAGAATTGAATTTAAGTTGTTGGTGACATCTGCATCATTTCATAGGATTAG AACTTACTCAAAATAATGTAAATCTTTAAAAATATAAATTAGAATGACAAGTGGGAATCATAA ATTAAACGTTAATGGTTTCTTATGCTCTTTTTAAATATAGAAATATCATGTTAAAGAAAAAAA AAAAAA

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FIGURE 302

MGFLSPIYVIFFFFGVKVHCQYETYQWDEDYDQEPDDDYQTGFPFRQNVDYGVPFHQYTLGCV SECFCPTNFPSSMYCDNRKLKTIPNIPMHIQQLYLQFNEIEAVTANSFINATHLKEINLSHNK IKSQKIDYGVFAKLPNLLQLHLEHNNLEEFPFPLPKSLERLLLGYNEISKLQTNAMDGLVNLT MLDLCYNYLHDSLLKDKIFAKMEKLMQLNLCSNRLESMPPGLPSSLMYLSLENNSISSIPEKY FDKLPKLHTLRMSHNKLQDIPYNIFNLPNIVELSVGHNKLKQAFYIPRNLEHLYLQNNEIEKM NLTVMCPSIDPLHYHHLTYIRVDQNKLKEPISSYIFFCFPHIHTIYYGEQRSTNGQTIQLKTQ VFRRFPDDDDESEDHDDPDNAHESPEQEGAEGHFDLHYYENQE

Important feastures:

N-glycosylation sites:

Amino acids 113-117;121-125; 187-191;242-246;316-320

Tyrosine kinase phosphorylation sites:

Amino acids 268-275;300-307

N-myristoylation site:

Amino acids 230-236

Leucine zipper patterns:

Amino acids 146-168;217-239

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FIGURE 303

GCCCGGGACTGGCGCAAGGTGCCCAAGCAAGGAAAGAATAATGAAGAGACACATGTGTTAGC TGCAGCCTTTTGAAACACGCAAGAAGGAAATCAATAGTGTGGACAGGGCTGGAACCTTTACCA CGCTTGTTGGAGTAGATGAGGAATGGGCTCGTGATTATGCTGACATTCCAGC**ATG**AATCTGGT AGACCTGTGGTTAACCCGTTCCCTCTCCATGTGTCTCCTCCTACAAAGTTTTGTTCTTATGAT ACTGTGCTTTCATTCTGCCAGTATGTGTCCCAAGGGCTGTCTTTGTTCTTCCTCTGGGGGTTT AAATGTCACCTGTAGCAATGCAAATCTCAAGGAAATACCTAGAGATCTTCCTCCTGAAACAGT CTTACTGTATCTGGACTCCAATCAGATCACATCTATTCCCAATGAAATTTTTAAGGACCTCCA TCAACTGAGAGTTCTCAACCTGTCCAAAAATGGCATTGAGTTTATCGATGAGCATGCCTTCAA AGGAGTAGCTGAAACCTTGCAGACTCTGGACTTGTCCGACAATCGGATTCAAAGTGTGCACAA AAATGCCTTCAATAACCTGAAGGCCAGGGCCAGAATTGCCAACAACCCCTGGCACTGCGACTG TACTCTACAGCAAGTTCTGAGGAGCATGGCGTCCAATCATGAGACAGCCCACAACGTGATCTG TAAAACGTCCGTGTTGGATGAACATGCTGGCAGACCATTCCTCAATGCTGCCAACGACGCTGA CCTTTGTAACCTCCCTAAAAAAACTACCGATTATGCCATGCTGGTCACCATGTTTGGCTGGTT CACTATGGTGATCTCATATGTGGTATATTATGTGAGGCAAAATCAGGAGGATGCCCGGAGACA CCTCGAATACTTGAAATCCCTGCCAAGCAGGCAGAAGAAGCAGATGAACCTGATGATATTAG GTAGAAATAAGTGGTTTACTTCTCCCATCCATTGTAAACATTTGAAACTTTGTATTTCAGTTT GTGATCCACCCCTTAATTGTACCCCCGATGGTATATTTCTGAGTAAGCTACTATCTGAACATT AGTTAGATCCATCTCACTATTTAATAATGAAATTTATTTTTTTAATTTAAAAGCAAATAAAAG

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FIGURE 304

MNLVDLWLTRSLSMCLLLQSFVLMILCFHSASMCPKGCLCSSSGGLNVTCSNANLKEIPRDLP
PETVLLYLDSNQITSIPNEIFKDLHQLRVLNLSKNGIEFIDEHAFKGVAETLQTLDLSDNRIQ
SVHKNAFNNLKARARIANNPWHCDCTLQQVLRSMASNHETAHNVICKTSVLDEHAGRPFLNAA
NDADLCNLPKKTTDYAMLVTMFGWFTMVISYVVYYVRQNQEDARRHLEYLKSLPSRQKKADEP
DDISTVV

Important features:

Signal sequence:

Amino acids 1-33

Transmembrane domain:

Amino acids 204-219

N-glycosylation sites:

Amino acids 47-51;94-98

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 199-203

Casein kinase II phosphorylation site.

amino acids 162-166, 175-179

N-myristoylation sites:

Amino acids 37-43;45-51;110-116

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FIGURE 305

CGCCACCACTGCGGCCACCGCCA<u>ATG</u>AAACGCCTCCCGCTCCTAGTGGTTTTTTTCCACTTTGTTGAATTGTTCCT ATACTCAAAATTGCACCAAGACACCTTGTCTCCCAAATGCAAAATGTGAAATACGCAATGGAATTGAAGCCTGCT GCAGTAACCAAGACAGGTTTATCACTAATGATGGAACCGTCTGTATAGAAAATGTGAATGCAAACTGCCATTTAG ATAATGTCTGTATAGCTGCAAATATTAATAAAACTTTAACAAAAATCAGATCCATAAAAGAACCTGTGGCTTTGC TACAAGAAGTCTATAGAAATTCTGTGACAGATCTTTCACCAACAGATATAATTACATATATAGAAATATTAGCTG AATCATCTTCATTACTAGGTTACAAGAACAACACTATCTCAGCCAAGGACACCCTTTCTAACTCAACTCTTACTG AATTTGTAAAAACCGTGAATAATTTTGTTCAAAGGGATACATTTGTAGTTTGGGACAAGTTATCTGTGAATCATA GGAGAACACATCTTACAAAACTCATGCACACTGTTGAACAAGCTACTTTAAGGATATCCCAGAGCTTCCAAAAGA CCACAGAGTTTGATACAAATTCAACGGATATAGCTCTCAAAGTTTTCTTTTTTGATTCATATAACATGAAACATA TTCATCCTCATATGAATATGGATGGAGACTACATAAATATTTTCCAAAGAGAAAAGCTGCATATGATTCAAATG GCAATGTTGCAGTTGCATTTTTATATTATAAGAGTATTGGTCCTTTGCTTTCATCATCTGACAACTTCTTATTGA AACCTCAAAATTATGATAATTCTGAAGAGGGGAAAGAGTCATATCTTCAGTAATTTCAGTCTCAATGAGCTCAA ACCCACCCACATTATATGAACTTGAAAAAATAACATTTACATTAAGTCATCGAAAGGTCACAGATAGGTATAGGA GTCTATGTGCATTTTGGAATTACTCACCTGATACCATGAATGGCAGCTGGTCTTCAGAGGGCTGTGAGCTGACAT ACTCAAATGAGACCCACACCTCATGCCGCTGTAATCACCTGACACATTTTGCAATTTTGATGTCCTCTGGTCCTT CCATTGGTATTAAAGATTATAATATTCTTACAAGGATCACTCAACTAGGAATAATTATTTCACTGATTTGTCTTG CCATATGCATTTTTACCTTCTGGTTCTTCAGTGAAATTCAAAGCACCAGGACAACAATTCACAAAAATCTTTGCT TTGCCGGACTGCTACACTACTTCTTTTTAGCTGCTTTTTGCATGGATGTGCATTGAAGGCATACATCTCTATCTCA TTGTTGTGGGTGTCATCTACAACAAGGGATTTTTGCACAAGAATTTTTATATCTTTGGCTATCTAAGCCCAGCCG TGGTAGTTGGATTTCGGCAGCACTAGGATACAGATATTATGGCACAAACCAAAGTATGTTGGCTTAGCACCGAAA ACAACTTTATTTGGAGTTTTATAGGACCAGCATGCCTAATCATTCTTGTTAATCTCTTGGCTTTTGGAGTCATCA GAGGAGCCCTCGCTCTTCTGTTCCTTCTCGGCACCACCTGGATCTTTGGGGTTCTCCATGTTGTGCACGCATCAG TGGTTACAGCTTACCTCTTCACAGTCAGCAATGCTTTCCAGGGGATGTTCATTTTTTTATTCCTGTGTGTTTTTAT CTAGAAAGATTCAAGAAGAATATTACAGATTGTTCAAAAATGTCCCCTGTTGTTTTGGATGTTTAAGG<u>TAA</u>ACAT AGAGAATGGTGGATAATTACAACTGCACAAAAATAAAAATTCCAAGCTGTGGATGACCAATGTATAAAAATGACT CATCAAATTATCCAATTATTAACTACTAGACAAAAAGTATTTTAAATCAGTTTTTCTGTTTATGCTATAGGAACT GTAGATAATAAGGTAAAATTATGTATCATATAGATATACTATGTTTTTCTATGTGAAATAGTTCTGTCAAAAATA ACACGAGAAGTATATGAATGTCCTGAAGGAAACCACTGGCTTGATATTTCTGTGACTCGTGTTGCCTTTGAAACT AGTCCCCTACCACCTCGGTAATGAGCTCCATTACAGAAAGTGGAACATAAGAGAATGAAGGGGCAGAATATCAAA CAGTGAAAAGGGAATGATAAGATGTATTTTGAATGAACTGTTTTTTCTGTAGACTAGCTGAGAAATTGTTGACAT AAAATAAAGAATTGAAGAAACACATTTTACCATTTTGTGAATTGTTCTGAACTTAAATGTCCACTAAAACAACTT

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FIGURE 306

MKRLPLLVVFSTLLNCSYTQNCTKTPCLPNAKCEIRNGIEACYCNMGFSGNGVTICEDDNECGNLTQSCGENANC
TNTEGSYYCMCVPGFRSSSNQDRFITNDGTVCIENVNANCHLDNVCIAANINKTLTKIRSIKEPVALLQEVYRNS
VTDLSPTDIITYIEILAESSSLLGYKNNTISAKDTLSNSTLTEFVKTVNNFVQRDTFVVWDKLSVNHRRTHLTKL
MHTVEQATLRISQSFQKTTEFDTNSTDIALKVFFFDSYNMKHIHPHMNMDGDYINIFPKRKAAYDSNGNVAVAFL
YYKSIGPLLSSSDNFLLKPQNYDNSEEEERVISSVISVSMSSNPPTLYELEKITFTLSHRKVTDRYRSLCAFWNY
SPDTMNGSWSSEGCELTYSNETHTSCRCNHLTHFAILMSSGPSIGIKDYNILTRITQLGIIISLICLAICIFTFW
FFSEIQSTRTTIHKNLCCSLFLAELVFLVGINTNTNKLFCSIIAGLLHYFFLAAFAWMCIEGIHLYLIVVGVIYN
KGFLHKNFYIFGYLSPAVVVGFSAALGYRYYGTTKVCWLSTENNFIWSFIGPACLIILVNLLAFGVIIYKVFRHT
AGLKPEVSCFENIRSCARGALALLFLLGTTWIFGVLHVVHASVVTAYLFTVSNAFQGMFIFLFLCVLSRKIQEEY
YRLFKNVPCCFGCLR

Important features:

Signal peptide:

Amino acids 1-19

Transmembrane domain:

Amino acids 431-450;494-515;573-594;619-636;646-664

N-glycosylation sites:

Amino acids 15-19;21-25;64-68;74-78;127-131;177-181; 188-192;249-253;381-385;395-399

Glycosaminoglycan attachment site:

Amino acids 49-53

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 360-364

Tyrosine kinase phosphorylation sites:

Amino acids 36-44;670-677

N-myristoylation sites:

Amino acids 38-44;50-56;52-58;80-86;382-388;388-394; 434-440;480-486;521-527

Aspartic acid and asparagine hydroxylation site:

Amino acids 75-87

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FIGURE 307

CCAGGCCGGAGGCGACGCCCCAGCCGTCTAAACGGGAACAGCCCTGGCTGAGGGAGCTGCAGCGCAGCAGAGT ATCTGACGCCCCAGGTTGCGTAGGTGCGCACGAGGAGGTTTTCCCGGCAGCGAGGAGGTCCTGAGCAGCATGGC GGCCGGGCCGCGCAGGAGGAGAGCCTGTACCTATGGATCGATGCTCACCAGGCAAGAGTACTCATAGGATTTGA AGAAGATATCCTGATTGTTTCAGAGGGGAAAATGGCACCTTTTACACATGATTTCAGAAAAGCGCAACAGAGAAT ATTCCTGTCCTTGCGCTCCCTGGATAAAGGCATCATGGCAGATCCAACCGTCAATGTCCCTCTGCTGGGAACAGT GCCTCACAAGGCATCAGTTGTTCAAGTTGGTTTCCCATGTCTTGGAAAACAGGATGGGGTGGCAGCATTTGAAGT GGATGTGATTGTTATGAATTCTGAAGGCAACACCATTCTCCAAACACCTCAAAATGCTATCTTCTTTAAAACATG TCAACAAGCTGAGTGCCCAGGCGGTGCCGAAATGGAGGCTTTTGTAATGAAAGACGCATCTGCGAGTGTCCTGA TGGGTTCCACGGACCTCACTGTGAGAAAGCCCTTTGTACCCCACGATGTATGAATGGTGGACTTTGTGTGACTCC TGGTTTCTGCATCTGCCCACCTGGATTCTATGGAGTGAACTGTGACAAAGCAAACTGCTCAACCACCTGCTTTAA TGGAGGGACCTGTTTCTACCCTGGAAAATGTATTTGCCCTCCAGGACTAGAGGGAGAGCAGTGTGAAATCAGCAA ATGCCCACACCCTGTCGAAATGGAGGTAAATGCATTGGTAAAAGCAAATGTAAGTGTTCCAAAGGTTACCAGGG AGACCTCTGTTCAAAGCCTGTCTGCGAGCCTGGCTGTGGTGCACATGGAACCTGCCATGAACCCAACAAATGCCA AGGCGCCCAGCTCAGGCAGCACACGCCTTCACTTAAAAAGGCCGAGGAGCGGGGGATCCACCTGAATCCAATTA CATCTGGTGAACTCCGACATCTGAAACGTTTTAAGTTACACCAAGTTCATAGCCTTTGTTAACCTTTCATGTGTT GAATGTTCAAATAATGTTCATTACACTTAAGAATACTGGCCTGAATTTTATTAGCTTCATTATAAATCACTGAGC TGATATTTACTCTTCCTTTTAAGTTTTCTAAGTACGTCTGTAGCATGATGGTATAGATTTTCTTGTTTCAGTGCT TTGGGACAGATTTTATATTATGTCAATTGATCAGGTTAAAATTTTCAGTGTGTAGTTGGCAGATATTTTCAAAAT TACAATGCATTTATGGTGTCTGGGGGCAGGGGAACATCAGAAAGGTTAAATTGGGCAAAAATGCGTAAGTCACAA ATTTTTAAAAATTGCTCTTAATTTTTAAACTCTCAATACAATATATTTTGACCTTACCATTATTCCAGAGATTCA GTATTAAAAAAAAAAATTACACTGTGGTAGTGGCATTTAAACAATATAATATATTCTAAACACAATGAAATAG GGAATATAATGTATGAACTTTTTGCATTGGCTTGAAGCAATATAATATTGTAAACAAAACACAGCTCTTACCT AAAAAAA

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FIGURE 308

MARRSAFPAAALWLWSILLCLLALRAEAGPPQEESLYLWIDAHQARVLIGFEEDILIVSEGKM
APFTHDFRKAQQRMPAIPVNIHSMNFTWQAAGQAEYFYEFLSLRSLDKGIMADPTVNVPLLGT
VPHKASVVQVGFPCLGKQDGVAAFEVDVIVMNSEGNTILQTPQNAIFFKTCQQAECPGGCRNG
GFCNERRICECPDGFHGPHCEKALCTPRCMNGGLCVTPGFCICPPGFYGVNCDKANCSTTCFN
GGTCFYPGKCICPPGLEGEQCEISKCPQPCRNGGKCIGKSKCKCSKGYQGDLCSKPVCEPGCG
AHGTCHEPNKCQCQEGWHGRHCNKRYEASLIHALRPAGAQLRQHTPSLKKAEERRDPPESNYIW

Important features:

Signal sequence:

Amino acids 1-28

N-glycosylation sites:

Amino acids 88-92;245-249

Tyrosine kinase phosphorylation site:

Amino acids 370-378

N-myristoylation sites:

Amino acids 184-190;185-191;189-195;315-321

ATP/GTP-binding site motif A (P-loop):

Amino acids 285-293

EGF-like domain cysteine pattern signatures:

Amino acids 198-210;230-242;262-274;294-306;326-338

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FIGURE 309

CCCACGCGTCCGGTCTCGCTCGCTCGCGCAGCGGCAGCAGAGGTCGCGCACAGATGCGGG CTTGCAAGCTGGATGCCCTCTGTGGATGAAAG<u>ATG</u>TATCATGGAATGAACCCGAGCAATGGAG ATGGATTTCTAGAGCAGCAGCAGCAGCAGCAGCAGCAGCCCCCCAGAGACTCTTGGCCG ACCTTCAAGTGTGTGCTGACCCCGGCATTCCCGAGAATGGCTTCAGGACCCCCAGCGGAGGGG TTTTCTTTGAAGGCTCTGTAGCCCGATTTCACTGCCAAGACGGATTCAAGCTGAAGGGCGCTA CAAAGAGACTGTGTTTGAAGCATTTTAATGGAACCCTAGGCTGGATCCCAAGTGATAATTCCA TCTGTGTGCAAGAAGATTGCCGTATCCCTCAAATCGAAGATGCTGAGATTCATAACAAGACAT ATAGACATGGAGAGAAGCTAATCATCACTTGTCATGAAGGATTCAAGATCCGGTACCCCGACC TACACAATATGGTTTCATTATGTCGCGATGATGGAACGTGGAATAATCTGCCCATCTGTCAAG GCTGCCTGAGACCTCTAGCCTCTTCTAATGGCTATGTAAACATCTCTGAGCTCCAGACCTCCT TCCCGGTGGGGACTGTGATCTCCTATCGCTGCTTTCCCGGATTTAAACTTGATGGGTCTGCGT ATCTTGAGTGCTTACAAAACCTTATCTGGTCGTCCAGCCCACCCGGTGCCTTGCTCTGGAAG CCCAAGTCTGTCCACTACCTCCAATGGTGAGTCACGGAGATTTCGTCTGCCACCCGCGGCCTT GTGAGCGCTACAACCACGGAACTGTGGTGGAGTTTTACTGCGATCCTGGCTACAGCCTCACCA GCGACTACAAGTACATCACCTGCCAGTATGGAGAGTGGTTTCCTTCTTATCAAGTCTACTGCA TCAAATCAGAGCAAACGTGGCCCAGCACCCATGAGACCCTCCTGACCACGTGGAAGATTGTGG CGTTCACGGCAACCAGTGTGCTGCTGGTGCTGCTCGTCATCCTGGCCAGGATGTTCCAGA CCAAGTTCAAGGCCCACTTTCCCCCCAGGGGGCCTCCCCGGAGTTCCAGCAGTGACCCTGACT TTGTGGTGGTAGACGGCGTGCCCGTCATGCTCCCGTCCTATGACGAAGCTGTGAGTGGCGGCT TGAGTGCCTTAGGCCCCGGGTACATGGCCTCTGTGGGCCAGGGCTGCCCCTTACCCGTGGACG ACCAGAGCCCCCCAGCATACCCCGGCTCAGGGGACACGGACACAGGCCCAGGGGAGTCAGAAA CCTGTGACAGCGTCTCAGGCTCTTCTGAGCTGCTCCAAAGTCTGTATTCACCTCCCAGGTGCC AAGAGAGCACCCACCCTGCTTCGGACAACCCTGACATAATTGCCAGCACGGCAGAGGAGGTGG CATCCACCAGCCCAGGCATCCATCATGCCCACTGGGTGTTGTTCCTAAGAAAC<u>TGA</u>TTGATTA AAAAATTTCCCAAAGTGTCCTGAAGTGTCTCTTCAAATACATGTTGATCTGTGGAGTTGATTC CTTTCCTTCTCTTGGTTTTAGACAAATGTAAACAAAGCTCTGATCCTTAAAATTGCTATGCTG ATAGAGTGGTGAGGGCTGGAAGCTTGATCAAGTCCTGTTTCTTCTTGACACAGACTGATTAAA AATTAAAAGNAAAAA

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FIGURE 310

MYHGMNPSNGDGFLEQQQQQQQPQSPQRLLAVILWFQLALCFGPAQLTGGFDDLQVCADPGIP ENGFRTPSGGVFFEGSVARFHCQDGFKLKGATKRLCLKHFNGTLGWIPSDNSICVQEDCRIPQ IEDAEIHNKTYRHGEKLIITCHEGFKIRYPDLHNMVSLCRDDGTWNNLPICQGCLRPLASSNG YVNISELQTSFPVGTVISYRCFPGFKLDGSAYLECLQNLIWSSSPPRCLALEAQVCPLPPMVS HGDFVCHPRPCERYNHGTVVEFYCDPGYSLTSDYKYITCQYGEWFPSYQVYCIKSEQTWPSTH ETLLTTWKIVAFTATSVLLVLLLVILARMFQTKFKAHFPPRGPPRSSSSDPDFVVVDGVPVML PSYDEAVSGGLSALGPGYMASVGQGCPLPVDDQSPPAYPGSGDTDTGPGESETCDSVSGSSEL LQSLYSPPRCQESTHPASDNPDIIASTAEEVASTSPGIHHAHWVLFLRN

Important features:

Signal sequence:

amino acids 1-41

Transmembrane domain:

amino acids 325-344

N-glycosylation site.

amino acids 104-108, 134-138, 192-196

Casein kinase II phosphorylation site.

amino acids 8-12, 146-150, 252-256, 270-274, 313-317, 362-366, 364-368, 380-384, 467-471, 468-472

N-myristoylation site.

amino acids 4-10, 61-67, 169-175, 203-209, 387-393, 418-424, 478-484

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 394-405

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FIGURE 311

CAGCGCGTGGCCGCGCGCTGTGGGGACAGCATGAGCGGCGGTTGGATGGCGCAGGTTGGAG CGTGGCGAACAGGGGCTCTGGGCCTGGCGCTGCTGCTGCTCGGCCTCGGACTAGGCCTGG AGGCCGCCGCGAGCCCGTTTCCACCCCGACCTCTGCCCAGGCCGCAGGCCCCAGCTCAGGCT CGTGCCCACCCACCAGTTCCAGTGCCGCACCAGTGGCTTATGCGTGCCCCTCACCTGGCGCT GCGACAGGGACTTGGACTGCAGCGATGGCAGCGATGAGGAGGAGTGCAGGATTGAGCCATGTA CCCAGAAAGGGCAATGCCCACCGCCCCTGGCCTCCCCTGCCCCTGCACCGGCGTCAGTGACT GCTCTGGGGGAACTGACAAGAAACTGCGCAACTGCAGCCGCCTGGCCTAGCAGGCGAGC TCCGTTGCACGCTGAGCGATGACTGCATTCCACTCACGTGGCGCTGCGACGGCCACCCAGACT GTCCCGACTCCAGCGACGAGCTCGGCTGTGGAACCAATGAGATCCTCCCGGAAGGGGATGCCA CAACCATGGGGCCCCCTGTGACCCTGGAGAGTGTCACCTCTCTCAGGAATGCCACAACCATGG GGCCCCTGTGACCCTGGAGAGTGTCCCCTCTGTCGGGAATGCCACATCCTCCTCTGCCGGAG ACCAGTCTGGAAGCCCAACTGCCTATGGGGTTATTGCAGCTGCTGCGGTGCTCAGTGCAAGCC TGGTCACCGCCACCCTCCTCTTTTGTCCTGGCTCCGAGCCCAGGAGCGCCTCCGCCCACTGG GGTTACTGGTGGCCATGAAGGAGTCCCTGCTGCTGTCAGAACAGAAGACCTCGCTGCCC<u>TGA</u>G GACAAGCACTTGCCACCACCGTCACTCAGCCCTGGGCGTAGCCGGACAGGAGGAGAGCAGTGA TGCGGATGGGTACCCGGGCACACCAGCCCTCAGAGACCTGAGTTCTTCTGGCCACGTGGAACC TCGAACCCGAGCTCCTGCAGAAGTGGCCCTGGAGATTGAGGGTCCCTGGACACTCCCTATGGA GATCCGGGGAGCTAGGATGGGGAACCTGCCACAGCCAGAACTGAGGGGCTGGCCCCAGGCAGC TCCCAGGGGGTAGAACGGCCCTGTGCTTAAGACACTCCCTGCTGCCCCGTCTGAGGGTGGCGA TTAAAGTTGCTTC

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FIGURE 312

MSGGWMAQVGAWRTGALGLALLLLLGLGLGLEAAASPLSTPTSAQAAGPSSGSCPPTKFQCRT SGLCVPLTWRCDRDLDCSDGSDEEECRIEPCTQKGQCPPPPGLPCPCTGVSDCSGGTDKKLRN CSRLACLAGELRCTLSDDCIPLTWRCDGHPDCPDSSDELGCGTNEILPEGDATTMGPPVTLES VTSLRNATTMGPPVTLESVPSVGNATSSSAGDQSGSPTAYGVIAAAAVLSASLVTATLLLLSW LRAQERLRPLGLLVAMKESLLLSEQKTSLP

Important features:

Signal sequence:

Amino acids 1-30

Transmembrane domain:

Amino acids 231-248

N-glycosylation sites:

Amino acids 126-130;195-199;213-217

Casein kinase II phosphorylation site.

amino acids 84-88, 140-144, 161-165, 218-222

N-myristoylation sites:

Amino acids 3-9;10-16;26-32;30-36;112-118;166-172;212-218; 224-230;230-236;263-269

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 44-55

Leucine zipper pattern:

Amino acids 17-39

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FIGURE 313

TTGGCTCTGGGTGCCCAGCAGGGTCGTGGGCGCCGGGAGCTAGCACCGGGTCTGCACCTGCGGGGCATCCGGGAC GCGGGAGGCCGGTACTGCCAGGAGCAGGACCTGTGCTGCCGCGGCCGTGCCGACGACTGTGCCCTACCTG GGCGCCATCTGTTACTGTGACCTCTTCTGCAACCGCACGGTCTCCGACTGCTGCCCTGACTTCTGGGACTTCTGC TACTGGGACAACTGTAACCGTTGCACCTGCCAGGAGAACAGGCAGTGGCATGGTGGATCCAGACATGATCAAAGC CATCAACCAGGGCAACTATGGCTGGCAGGCTGGGAACCACAGCGCCTTCTGGGGCATGACCCTGGA<u>TGA</u>GGGCAT AGGGGAGGTGCTTCCCACAGCCTTCGAGGCCTCTGAGAAGTGGCCCAACCTGATTCATGAGCCTCTTGACCAAGG CAACTGTGCAGGCTCCTGGGCCTTCTCCACAGCAGCTGTGGCATCCGATCGTGTCTCAATCCATTCTCTGGGACA TCTCGATGGTGCCTGGTGGTTCCTGCGTCGCCGAGGGGTGTGTCTGACCACTGCTACCCCTTCTCGGGCCGTGA ACGAGACGAGGCTGGCCCTGCGCCCCCTGTATGATGCACAGCCGAGCCATGGGTCGGGGCAAGCGCCAGGCCAC TGCCCACTGCCCAACAGCTATGTTAATAACAATGACATCTACCAGGTCACTCCTGTCTACCGCCTCGGCTCCAA CGACAAGGAGATCATGAAGGAGCTGATGGAGAATGGCCCTGTCCAAGCCCTCATGGAGGTGCATGAGGACTTCTT CCTATACAAGGGAGGCATCTACAGCCACACGCCAGTGAGCCTTGGGAGGCCAGAGAGATACCGCCGGCATGGGAC CCACTCAGTCAAGATCACAGGATGGGGAGAGGAGACGCTGCCAGATGGAAGGACGCTCAAATACTGGACTGCGGC CAACTCCTGGGGCCCAGCCTGGGGCGAGAGGGGCCACTTCCGCATCGTGCGCGGCGTCAATGAGTGCGACATCGA GAGCTTCGTGCTGGGCGTCTGGGGCCGCGTGGGCATGGAGGACATGGGTCATCACTGAGGCTGCGGGCACCACGC GGGGTCCGGCCTGGGATCCAGGCTAAGGGCCGGCGGAAGAGGCCCCAATGGGGCGGTGACCCCAGCCTCGCCCGA CAGAGCCCGGGGCGCAGGCGCCCAGGGCGCTAATCCCGGCGGGTTCCGCTGACGCAGCGCCCCGCCTGGG AGCCGCGGGCAGGCGAGACTGGCGGAGCCCCCAGACCTCCCAGTGGGGACGGGCAGGGCCTGGCCTGGGAAGAG CACAGCTGCAGATCCCAGGCCTCTGGCGCCCCCACTCAAGACTACCAAAGCCAGGACACCTCAAGTCTCCAGCCC TGCAGTGGCCCATCAGGGCTCACTGTAACCTCCGACTCCTGGGTTCAAGTGACCCTCCCACCTCAGCCTCTCAAG TGCCCAGGCTGGTTTCGAACTCCTGGGCTCAAGCGGTCCACCTGCCTCCGCCTCCCAAAGTGCTGGGATTGCAGG CCAAAGTATTGATAAAAAAAAA

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FIGURE 314

MWRCPLGLLLLPLAGHLALGAQQGRGRRELAPGLHLRGIRDAGGRYCQEQDLCCRGRADDCA LPYLGAICYCDLFCNRTVSDCCPDFWDFCLGVPPPFPPIQGCMHGGRIYPVLGTYWDNCNRCT CQENRQWHGGSRHDQSHQPGQLWLAGWEPQRLLGHDPG

Important features:

N-glycosylation site.

amino acids 78-82, 161-165

Casein kinase II phosphorylation site.

amino acids 80-84, 117-121, 126-130, 169-173, 205-209, 296-300, 411-415

N-myristoylation site.

amino acids 21-27, 39-45, 44-50, 104-110, 160-164, 224-230, 269-275, 378-384, 442-448

Amidation site.

amino acids 26-30, 318-322

Eukaryotic thiol (cysteine) proteases histidine active site. amino acids 398-409

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FIGURE 315

 $\tt CGGACGCGTGGGCCCCTGGTGGGCCCAGCAAG{\color{red} \underline{\textbf{ATG}}} GATCTACTGTGGATCCTGCCCTCCTGT$ GGCTTCTCCTGCTTGGGGGGCCTGCCTGAAGACCCAGGAACACCCCAGCTGCCCAGGAC CCAGGGAACTGGAAGCCAGCAAAGTTGTCCTCCTGCCCAGTTGTCCCGGAGCTCCAGGAAGTC CTGGGGAGAGGGGCCCCAGGTCCTCAAGGGCCACCTGGACCACCAGGCAAGATGGGCCCCA AGGGTGAGCCAGGCCCCAGAAACTGCCGGGAGCTGTTGAGCCAGGGCGCCACCTTGAGCGGCT GGTACCATCTGTGCCTACCTGAGGGCAGGGCCCTCCCAGTCTTTTGTGACATGGACACCGAGG GGGGCGCTGGCTGTTTCAGAGGCGCCAGGATGGTTCTGTGGATTTCTTCCGCTCTTGGT ACCAGCTTACTCTCCAGGGTAACTGGGAGCTGCGGGTAGAGCTTGGAAGACTTTAATGGTAACC GTACTTTCGCCCACTATGCGACCTTCCGCCTCCTCGGTGAGGTAGACCACTACCAGCTGGCAC TGGGCAAGTTCTCAGAGGGCACTGCAGGGGATTCCCTGAGCCTCCACAGTGGGAGGCCCTTTA CCACCTATGACGCTGACCACGATTCAAGCAACAGCAACTGTGCAGTGATTGTCCACGGTGCCT GGTGGTATGCATCCTGTTACCGATCAAATCTCAATGGTCGCTATGCAGTGTCTGAGGCTGCCG CCCACAAATATGGCATTGACTGGGCCTCAGGCCGTGGTGTGGGCCACCCCTACCGCAGGGTTC GGATGATGCTTCGA<u>TAG</u>GGCACTCTGGCAGCCAGTGCCCTTATCTCTCTGTACAGCTTCCGG ATCGTCAGCCACCTTGCCTTTGCCAACCACCTCTGCTTGCCTGTCCACATTTAAAAATAAAAT CATTTTAGCCCTTTCA

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FIGURE 316

MDLLWILPSLWLLLLGGPACLKTQEHPSCPGPRELEASKVVLLPSCPGAPGSPGEKGAPGPQG
PPGPPGKMGPKGEPGPRNCRELLSQGATLSGWYHLCLPEGRALPVFCDMDTEGGGWLVFQRRQ
DGSVDFFRSWSSYRAGFGNQESEFWLGNENLHQLTLQGNWELRVELEDFNGNRTFAHYATFRL
LGEVDHYQLALGKFSEGTAGDSLSLHSGRPFTTYDADHDSSNSNCAVIVHGAWWYASCYRSNL
NGRYAVSEAAAHKYGIDWASGRGVGHPYRRVRMMLR

Important features:

Signal peptide:

Amino acids 1-16

N-glycosylation site:

Amino acids 178-182

Glycosaminoglycan attachment site:

Amino acids 272-276

Tyrosine kinase phosphorylation site:

Amino acids 188-197

N-myristoylation sites:

Amino acids 16-22;89-95;144-150;267-273

Fibrinogen beta and gamma chains C-terminal domain signature:

Amino acids.242-255

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FIGURE 317

CCCAAGCCAGCCGAGCCGCAGAGCCGCGGGGCCGGGGGTGTCGCGGGCCCAACCCCAGGAT **G**CTCCCCTGCGCCTCCTGCCTACCCGGGTCTCTACTGCTCTGGGCGCTGCTACTGTTGCTCTT GGGATCAGCTTCTCCTCAGGATTCTGAAGAGCCCGACAGCTACACGGAATGCACAGATGGCTA TGAGTGGGACCCAGACAGCCAGCACTGCCGGGATGTCAACGAGTGTCTGACCATCCCTGAGGC TGCCGTCATCAACGACCTACATGGCGAGGGACCCCCGCCACCAGTGCCTCCCGCTCAACACCC CAACCCTGCCCACCAGGCTATGAGCCCGACGATCAGGACAGCTGTGTGGATGTGGACGAGTG TGCCCAGGCCCTGCACGACTGTCGCCCCAGCCAGGACTGCCATAACTTGCCTGGCTCCTATCA GTGCACCTGCCCTGATGGTTACCGCAAGATCGGGCCCGAGTGTGTGGACATAGACGAGTGCCG CTACCGCTACTGCCAGCACCGCTGCGTGAACCTGCCTGGCTCCTTCCGCTGCCAGTGCGAGCC GGGCTTCCAGCTGGGGCCTAACAACCGCTCCTGTGTTGATGTGAACGAGTGTGACATGGGGGC CCCATGCGAGCAGCGCTGCTTCAACTCCTATGGGACCTTCCTGTGTCGCTGCCACCAGGGCTA TGAGCTGCATCGGGATGGCTTCTCCTGCAGTGATATTGATGAGTGTAGCTACTCCAGCTACCT CTGTCAGTACCGCTGCGTCAACGAGCCAGGCCGTTTCTCCTGCCACTGCCCACAGGGTTACCA GCTGCTGGCCACACGCCTCTGCCAAGACATTGATGAGTGTGAGTCTGGTGCGCACCAGTGCTC CGAGGCCCAAACCTGTGTCAACTTCCATGGGGGCTACCGCTGCGTGGACACCAACCGCTGCGT GGAGCCCTACATCCAGGTCTCTGAGAACCGCTGTCTCTGCCCGGCCTCCAACCCTCTATGTCG AGAGCAGCCTTCATCCATTGTGCACCGCTACATGACCATCACCTCGGAGCGGAGCGTGCCCGC TGACGTGTTCCAGATCCAGGCGACCTCCGTCTACCCCGGTGCCTACAATGCCTTTCAGATCCG TGCTGGAAACTCGCAGGGGGACTTTTACATTAGGCAAATCAACAACGTCAGCGCCATGCTGGT CCTCGCCCGGCCGGTGACGGCCCCCGGGAGTACGTGCTGGACCTGGAGATGGTCACCATGAA TTCCCTCATGAGCTACCGGGCCAGCTCTGTACTGAGGGCTCACCGTCTTTGTAGGGGCCTACAC CTTCTGAGGAGCAGGAGCCACCCTCCCTGCAGCTACCCTAGCTGAGGAGCCTGTTGTGA GGGGCAGAATGAGAAAGGCAATAAAGGGAGAAAGAAAGTCCTGGTGGCTGAGGTGGGCGGGTC ACACTGCAGGAAGCCTCAGGCTGGGGCAGGTGGCACTTGGGGGGGCAGGCCAAGTTCACCTA AATGGGGGTCTCTATATGTTCAGGCCCAGGGGCCCCCATTGACAGGAGCTGGGAGCTCTGCAC CACGAGCTTCAGTCACCCCGAGAGGAGGAGGAGGTAACGAGGAGGCGGACTCCAGGCCCCGGC CCAGAGATTTGGACTTGCTGGCTTGCAGGGGTCCTAAGAAACTCCACTCTGGACAGCGCCAG GAGGCCCTGGGTTCCATTCCTAACTCTGCCTCAAACTGTACATTTGGATAAGCCCTAGTAGTT

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FIGURE 318

MLPCASCLPGSLLLWALLLLLLGSASPQDSEEPDSYTECTDGYEWDPDSQHCRDVNECLTIPE
ACKGEMKCINHYGGYLCLPRSAAVINDLHGEGPPPPVPPAQHPNPCPPGYEPDDQDSCVDVDE
CAQALHDCRPSQDCHNLPGSYQCTCPDGYRKIGPECVDIDECRYRYCQHRCVNLPGSFRCQCE
PGFQLGPNNRSCVDVNECDMGAPCEQRCFNSYGTFLCRCHQGYELHRDGFSCSDIDECSYSSY
LCQYRCVNEPGRFSCHCPQGYQLLATRLCQDIDECESGAHQCSEAQTCVNFHGGYRCVDTNRC
VEPYIQVSENRCLCPASNPLCREQPSSIVHRYMTITSERSVPADVFQIQATSVYPGAYNAFQI
RAGNSQGDFYIRQINNVSAMLVLARPVTGPREYVLDLEMVTMNSLMSYRASSVLRLTVFVGAYTF

Important features:

Signal sequence:

Amino acids 1-25

N-glycosylation sites:

Amino acids 198-202;394-398

N-myristoylation sites:

Amino acids 76-82;145-151;182-188;222-228;290-296;305-311; 371-377;381-387

Aspartic acid and asparagine hydroxylation sites:

amino acids 140-152;177-189;217-229;258-270

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FIGURE 319

TCAAAGGTGCGTACCCAGCTGTGCCCGACACCATGTACCTGCCCCTGGCCACCTCCCCGATGC CCGCTGGGAGTACCCCTGGTGCTGGATGGCTGTGGCTGCCGGGTATGTGCACGGCGGCTG GCAGGACCCGGTGGCCGGGGGCCCTGTGCCTCTTGGCAGAGGACGACAGCAGCTGTGAGGTG AACGGCCGCCTGTATCGGGAAGGGGAGACCTTCCAGCCCCACTGCAGCATCCGCTGCCGCTGC GAGGACGGCGGCTTCACCTGCGTGCCGCTGTGCAGCGAGGATGTGCGGCTGCCCAGCTGGGAC TGCCCCCACCCAGGAGGGTCGAGGTCCTGGGCAAGTGCTGCCCTGAGTGGGTGTGCGGCCAA GGAGGGGGACTGGGGACCCAGCCCCTTCCAGCCCAAGGACCCCAGTTTTCTGGCCTTGTCTCT TCCCTGCCCCTGGTGTCCCCTGCCCAGAATGGAGCACGGCCTGGGGGACCCTGCTCGACCACC TGTGGGCTGGGCATGGCCACCGGGTGTCCAACCAGAACCGCTTCTGCCGACTGGAGACCCAG CGCCGCCTGTGCCTGTCCAGGCCCTGCCCACCCTCCAGGGGTCGCAGTCCACAAAACAGTGCC TGGGCCCTGGGCTGATGGAAGATGGTCCGTGCCCAGGCCCTTGGCTGCAGGCAACACTTTAGC TGGCAGAGGTGCAAGACCTAGTCCCCTTTCCTCTAACTCACTGCCTAGGAGGCTGGCCAAGGT CGAGCTTTCTCCCGACTTCCCCTGGGCAAGAGATGGGACAAGCAGTCCCTTAATATTGAGGC TGCAGCAGGTGCTGGGCTGGACTGGCCATTTTTCTGGGGGTAGGATGAAGAAGGCACACAG AGATTCTGGATCTCCTGCTGCCTTTTCTGGAGTTTGTAAAATTGTTCCTGAATACAAGCCTAT GCGTGA

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FIGURE 320

MRGTPKTHLLAFSLLCLLSKVRTQLCPTPCTCPWPPPRCPLGVPLVLDGCGCCRVCARRLGEP CDQLHVCDASQGLVCQPGAGPGGRGALCLLAEDDSSCEVNGRLYREGETFQPHCSIRCRCEDG GFTCVPLCSEDVRLPSWDCPHPRRVEVLGKCCPEWVCGQGGGLGTQPLPAQGPQFSGLVSSLP PGVPCPEWSTAWGPCSTTCGLGMATRVSNQNRFCRLETQRRLCLSRPCPPSRGRSPQNSAF

Important features:

Signal sequence:

Amino acids 1-23

N-myristoylation sites:

Amino acids 3-9;49-55;81-87;85-91;126-132;164-170;166-172; 167-173;183-189;209-215

Insulin-like growth factor binding proteins signature:

Amino acids 49-65

von Willebrand C1 domain:

Amino acids 107-124

Thrombospondin 1 Homology Block:

Amino acids 201-216

IGF binding protein site:

Amino acids 49-58

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FIGURE 321

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FIGURE 322

MMGLSLASAVLLASLLSLHLGTATRGSDISKTCCFQYSHKPLPWTWVRSYEFTSNSCSQRAVI FTTKRGKKVCTHPRKKWVQKYISLLKTPKQL

Important features:

Signal peptide:

amino acids 1-23

N-myristoylation sites.

amino acids 3-9, 26-32

Amidation site.

amino acids 68-72

Small cytokines (intecrine/chemokine).

amino acids 23-88

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FIGURE 323

ACCGAGCCGAGCGGACCGAAGGCGCCCCCGAGATGCAGGTGAGCAAGAGGATGCTGGCGGGGGGCGTGAGGAGCA TGCCCAGCCCCTCCTGGCCTGCTGGCAGCCCATCCTCCTGCTGGTGCTGGGCTCAGTGCTGTCAGGCTCAGCCCA CGGGCTGCCCCCCCGCTGCGAGTGCTCCGCCCAGGACCGCGCTGTGCTGTGCCACCGCAAGTGCTTTGTGGCAG TCCCCGAGGGCATCCCCACCGAGACGCGCCTGCTGGACCTAGGCAAGAACCGCATCAAAACGCTCAACCAGGACG AGTTCGCCAGCTTCCCGCACCTGGAGGAGCTGGAGCTCAACGAGAACATCGTGAGCGCCGTGGAGCCCGGCGCCCT TCAACAACCTCTTCAACCTCCGGACGCTGGGTCTCCGCAGCAACCGCCTGAAGCTCATCCCGCTAGGCGTCTTCA CTGGCCTCAGCAACCTGACCAAGCAGGACATCAGCGAGAACAAGATCGTTATCCTACTGGACTACATGTTTCAGG ACCTGTACAACCTCAAGTCACTGGAGGTTGGCGACAATGACCTCGTCTACATCTCTCACCGCGCCTTCAGCGGCC TCAACAGCCTGGAGCAGCTGACGCTGGAGAAATGCAACCTGACCTCCATCCCACCGAGGCGCTGTCCCACCTGC ACGGCCTCATCGTCCTGAGGCTCCGGCACCTCAACATCAATGCCATCCGGGACTACTCCTTCAAGAGGCTGTACC GACTCAAGGTCTTGGAGATCTCCCACTGGCCCTACTTGGACACCATGACACCCAACTGCCTCTACGGCCTCAACC TGACGTCCCTGTCCATCACACACTGCAATCTGACCGCTGTGCCCTACCTGGCCGTCCGCCACCTAGTCTATCTCC GCTTCCTCAACCTCTACAACCCCATCAGCACCATTGAGGGCTCCATGTTGCATGAGCTGCTCCGGCTGCAGG AGATCCAGCTGGTGGGCGGCCAGCTGGCCGTGGTGGAGCCCTATGCCTTCCGCGGCCTCAACTACCTGCGCGTGC TCAATGTCTCTGGCAACCAGCTGACCACACTGGAGGAATCAGTCTTCCACTCGGTGGGCAACCTGGAGACACTCA ${\tt TCCTGGACTCCAACCCGCTGGCCTGCGACTGTCGGCTCCTGTGGGTGTTCCGGCGCGCTGGCGGCTCAACTTCA}$ ACCGGCAGCAGCCCACGTGCGCCACGCCCGAGTTTGTCCAGGGCAAGGAGTTCAAGGACTTCCCTGATGTGCTAC $\tt TGGTCTCAGCCAAGAGCAATGGGCGGCTCACAGTCTTCCCTGATGGCACGCTGGAGGTGCGCTACGCCCAGGTAC$ GCAGCTACTCGCCCGACTGGCCCCATCAGCCCAACAAGACCTTCGCTTTCATCTCCAACCAGCCGGGCGAGGGAG AGGCCAACAGCACCGCGCCACTGTGCCTTTCCCCTTCGACATCAAGACCCTCATCATCGCCACCACCATGGGCT ${\tt AGCACAACATCGAGATCGAGTATGTGCCCCGAAAGTCGGACGCAGGCATCAGCTCCGCCGACGCGCCCCGCAAGT}$ ${\tt TCCGTCCCTGCTGCCCCCGCCAGCCCTCACCACCTGCCCTCTTCTACCAGGACCTCAGAAGCCCAGACCTGG}$ GGACCCCACCTACACAGGGGCATTGACAGACTGGAGTTGAAAGCCGACGACGACACGCGGCAGAGTCAATAAT TCAATAAAAAGTTACGAACTTTCTCTGTAACTTGGGTTTCAATAATTATGGATTTTTATGAAAACTTGAAATAA

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FIGURE 324

MQVSKRMLAGGVRSMPSPLLACWQPILLLVLGSVLSGSATGCPPRCECSAQDRAVLCHRKCFVAVPEGIPTETRL LDLGKNRIKTLNQDEFASFPHLEELELNENIVSAVEPGAFNNLFNLRTLGLRSNRLKLIPLGVFTGLSNLTKQDI SENKIVILLDYMFQDLYNLKSLEVGDNDLVYISHRAFSGLNSLEQLTLEKCNLTSIPTEALSHLHGLIVLRLRHL NINAIRDYSFKRLYRLKVLEISHWPYLDTMTPNCLYGLNLTSLSITHCNLTAVPYLAVRHLVYLRFLNLSYNPIS TIEGSMLHELLRLQEIQLVGGQLAVVEPYAFRGLNYLRVLNVSGNQLTTLEESVFHSVGNLETLILDSNPLACDC RLLWVFRRRWRLNFNRQQPTCATPEFVQGKEFKDFPDVLLPNYFTCRRARIRDRKAQQVFVDEGHTVQFVCRADG DPPPAILWLSPRKHLVSAKSNGRLTVFPDGTLEVRYAQVQDNGTYLCIAANAGGNDSMPAHLHVRSYSPDWPHQP NKTFAFISNQPGEGEANSTRATVPFPFDIKTLIIATTMGFISFLGVVLFCLVLLFLWSRGKGNTKHNIEIEYVPR KSDAGISSADAPRKFNMKMI

Important features:

Signal sequence:

amino acids 1-41

Transmembrane domain:

amino acids 556-578

N-glycosylation site.

amino acids 144-148, 202-206, 264-268, 274-278, 293-297, 341-345, 492-496, 505-509, 526-530, 542-546

Casein kinase II phosphorylation site.

amino acids 49-53, 108-112, 146-150, 300-304, 348-352, 349-353, 607-611

Tyrosine kinase phosphorylation site.

amino acids 590-598

N-myristoylation site.

amino acids 10-16, 32-38, 37-43, 113-119, 125-131, 137-143, 262-268, 320-326, 344-350, 359-365, 493-499, 503-509, 605-611

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 32-43

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FIGURE 325

GAGATGCGGGATGGAGACCTGGAGTTAGGTGGCTTGGGAGAGCTTAATGAAAAGAGAACGGAG AGGAGGTGTGGGTTAGGAACCAAGAGGTAGCCCTGTGGGCAGCAGAAGGCTGAGAGGAGTAGG AAGATCAGGAGCTAGAGGGAGACTGGAGGGTTCCGGGAAAAGAGCAGAGGAAAGAGGAAAGAC ACAGAGAGACGGGAGAGAGAGAGAGGGTTTTGAAGGGCGGATCTCAGTCCCTGGCTGCTT TGGCATTTGGGGAACTGGGACTCCCTGTGGGGAGGAGGGAAAGCTGGAAGTCCTGGAGGGAC AGGGTCCCAGAAGGAGGGGCACAGAGGGGGCGTTGGGCAGGGGTCC CTCGGAGGCCTCCTGGGGATGGGGGCTGCAGCTCGTCTGAGCGCCCCTCGAGCGCTGGTACTC TGGGCTGCACTGGGGGCAGCAGCTCACATCGGACCAGCACCTGACCCCGAGGACTGGTGGAGC TACAAGGATAATCTCCAGGGAAACTTCGTGCCAGGGCCTCCTTTCTGGGGCCTGGTGAATGCA GCGTGGAGTCTGTGTGCTGTGGGGAAGCGGCAGAGCCCCGTGGATGTGGAGCTGAAGAGGGTT CTTTATGACCCCTTTCTGCCCCCATTAAGGCTCAGCACTGGAGGAGAAGCTCCGGGGAACC TTGTACAACACCGGCCGACATGTCTCCTTCCTGCCTGCACCCCGACCTGTGGTCAATGTGTCT GGAGGTCCCCTCCTTTACAGCCACCGACTCAGTGAACTGCGGCTGCTGTTTGGAGCTCGCGAC GGAGCCGGCTCGGAACATCAGATCAACCACCAGGGCTTCTCTGCTGAGGTGCAGCTCATTCAC TTCAACCAGGAACTCTACGGGAATTTCAGCGCTGCCTCCCGCGGCCCCAATGGCCTGGCCATT CTCAGCCTCTTTGTCAACGTTGCCAGTACCTCTAACCCATTCCTCAGTCGCCTCCTTAACCGC GACACCATCACTCGCATCTCCTACAAGAATGATGCCTACTTTCTTCAAGACCTGAGCCTGGAG CTCCTGTTCCCTGAATCCTTCGGCTTCATCACCTATCAGGGCTCTCTCAGCACCCCGCCCTGC TCCGAGACTGTCACCTGGATCCTCATTGACCGGGCCCTCAATATCACCTCCCTTCAGATGCAC TCCCTGAGACTCCTGAGCCAGATCCTCCATCTCAGATCTTCCAGAGCCTCAGCGGTAACAGC CGGCCCTGCAGCCCTTGGCCCACAGGGCACTGAGGGGCACAGGGACCCCCGGCACCCCGAG AGGCGCTGCCGAGGCCCCAACTACCGCCTGCATGTGGATGGTGTCCCCCATGGTCGC<u>TGA</u>GAC TCCCCTTCGAGGATTGCACCCGCCCGTCCTAAGCCTCCCCACAAGGCGAGGGGAGTTACCCCT AAAACAAAGCTATTAAAGGGACAGAATACTTA

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FIGURE 326

MGAAARLSAPRALVLWAALGAAAHIGPAPDPEDWWSYKDNLQGNFVPGPPFWGLVNAAWSLCA
VGKRQSPVDVELKRVLYDPFLPPLRLSTGGEKLRGTLYNTGRHVSFLPAPRPVVNVSGGPLLY
SHRLSELRLLFGARDGAGSEHQINHQGFSAEVQLIHFNQELYGNFSAASRGPNGLAILSLFVN
VASTSNPFLSRLLNRDTITRISYKNDAYFLQDLSLELLFPESFGFITYQGSLSTPPCSETVTW
ILIDRALNITSLQMHSLRLLSQNPPSQIFQSLSGNSRPLQPLAHRALRGNRDPRHPERRCRGP
NYRLHVDGVPHGR

Important features:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 177-199

N-glycosylation sites:

Amino acids 118-122;170-174;260-264

Eukaryotic-type carbonic anhydrases proteins:

Amino acids 222-271;128-165;45-93

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FIGURE 327

GGACTAATCTGTGGGAGCAGTTTATTCCAGTATCACCCAGGGTGCAGCCACACCAGGACTGTGTTGAAGGGTGTT TTTTTTTTTTAAATGTAATACCTCCTCATCTTTTCTTCTTACACAGTGTCTGAGAACATTTACATTATAGATAA GTAGTACATGGTGGATAACTTCTACTTTTAGGAGGACTACTCTCTTCTGACAGTCCTAGACTGGTCTTCTACACT AAGACACCATGAAGGAGTATGTGCTCCTATTATTCCTGGCTTTGTGCTCCCAAACCCTTCTTTAGCCCTTCAC ATGATGATGAGGACAACTCTCTTTTTCCAACAAGAGGCCAAGAAGCCATTTTTTTCCATTTGATCTGTTTCCAA TGTGTCCATTTGGATGTCAGTGCTATTCACGAGTTGTACATTGCTCAGATTTAGGTTTGACCTCAGTCCCAACCA ACATTCCATTTGATACTCGAATGCTTGATCTTCAAAACAATAAAATTAAGGAAATCAAAGAAAATGATTTTAAAG GACTCACTTCACTTTATGGTCTGATCCTGAACAACAACAAGCTAACGAAGATTCACCCAAAAGCCTTTCTAACCA CAAAGAAGTTGCGAAGGCTGTATCTGTCCCACAATCAACTAAGTGAAATACCACTTAATCTTCCCAAATCATTAG TTTTGGAAATGAGTGCAAACCCTCTTGATAATAATGGGATAGAGCCAGGGGCATTTGAAGGGGTGACGGTGTTCC ATATCAGAATTGCAGAAGCAAAACTGACCTCAGTTCCTAAAGGCTTACCACCAACTTTATTGGAGCTTCACTTAG ATTATAAAAATTTCAACAGTGGAACTTGAGGATTTTAAACGATACAAAGAACTACAAAGGCTGGGCCTAGGAA ACAACAAAATCACAGATATCGAAAATGGGAGTCTTGCTAACATACCACGTGTGAGAAAATACATTTGGAAAACA TTGCAAGAGTGGGAGTAAATGACTTCTGTCCAACAGTGCCAAAGATGAAGAAATCTTTATACAGTGCAATAAGTT TATTCAACAACCCGGTGAAATACTGGGAAATGCAACCTGCAACATTTCGTTGTTGTTTTGAGCAGAATGAGTGTTC AGCTTGGGAACTTTGGAATG<u>TAA</u>TAATTAGTAATTGGTAATGTCCATTTAATATAGGATTCAAAAAATCCCTACAT ACTGACTTATTTTATGACAAGAAATTTCAACGGAATTTTGCCAAACTATTGATACATAAGGGGTTGAGAGAAACA AGCATCTATTGCAGTTTCCTTTTTGCGTACAAATGATCTTACATAAATCTCATGCTTGACCATTCCTTTCTTCAT AACAAAAAGTAAGATATTCGGTATTTAACACTTTGTTATCAAGCACATTTTAAAAAGAACTGTACTGTAAATGG AATGCTTGACTTAGCAAAATTTGTGCTCTTTCATTTGCTGTTAGAAAAACAGAATTAACAAAGACAGTAATGTGA AGAGTGCATTACACTATTCTTATTCTTTAGTAACTTGGGTAGTACTGTAATATTTTTAATCATCTTAAAGTATGA TTTGATATATCTTATTGAAATTACCTTATCATGTCTTAGAGCCCGTCTTTATGTTTAAAACTAATTTCTTAAAA TAAAGCCTTCAGTAAATGTTCATTACCAACTTGATAAATGCTACTCATAAGAGCTGGTTTGGGGCTATAGCATAT GCTTTTTTTTTTTAATTATTACCTGATTTAAAAATCTCTGTAAAAACGTGTAGTGTTTCATAAAATCTGTAACT CGCATTTTAATGATCCGCTATTATAAGCTTTTAATAGCATGAAAATTGTTAGGCTATATAACATTGCCACTTCAA AAATTGTCTCTTCAAATACGTATGGACTGGATAACTCTGAGAAACACATCTAGTATAACTGAATAAGCAGAGCAT CAAATTAAACAGACAGAAACCGAAAGCTCTATATAAATGCTCAGAGTTCTTTATGTATTTCTTATTGGCATTCAA CATATGTAAAATCAGAAAACAGGGAAATTTTCATTAAAAATATTGGTTTGAAAT

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FIGURE 328

Important features:

Signal sequence.

amino acids 1-15

N-glycosylation site.

amino acids 281-285

N-myristoylation sites.

amino acids 129-135, 210-216, 214-220, 237-243, 270-276, 282-288

Leucine zipper pattern.

amino acids 154-176

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FIGURE 329

TCCGCAGGTTCCCGCGGACTTGGGGGCCCCGCTGAGCCCCGGCGCCCCCAGAAGACTTGTGT TTGCCTCCTGCAGCCTCAACCCGGAGGGCAGCGAGGGCCTACCACCATGATCACTGGTGTGTT GCGGGTGGCCCTGGCCGAGCTGCAGGAGGCCGATGGCCAGTGTCCGGTCGACCGCAGCCTGCT GAAGTTGAAAATGGTGCAGGTCGTGTTTCGACACGGGGCTCGGAGTCCTCTCAAGCCGCTCCC GCTGGAGGAGCAGGTAGAGTGGAACCCCCAGCTATTAGAGGTCCCACCCCAAACTCAGTTTGA TTACACAGTCACCAATCTAGCTGGTGGTCCGAAACCATATTCTCCTTACGACTCTCAATACCA TGAGACCACCCTGAAGGGGGGCATGTTTGCTGGGCAGCTGACCAAGGTGGGCATGCAGCAAAAT CTTCAACCCACAGGAGGTCTTTATTCGTTCCACTAACATTTTTCGGAATCTGGAGTCCACCCG TTGTTTGCTGGCTGGGCTTTTCCAGTGTCAGAAAGAAGGACCCATCATCATCCACACTGATGA AGCAGATTCAGAAGTCTTGTATCCCAACTACCAAAGCTGCTGGAGCCTGAGGCAGAGAACCAG AGGCCGGAGGCAGACTGCCTCTTTACAGCCAGGAATCTCAGAGGATTTGAAAAAAGGTGAAGGA CAGGATGGGCATTGACAGTAGTGATAAAGTGGACTTCTTCATCCTCCTGGACAACGTGGCTGC CGAGCAGGCACACCTCCCAAGCTGCCCCATGCTGAAGAGATTTGCACGGATGATCGAACA GAGAGCTGTGGACACATCCTTGTACATACTGCCCAAGGAAGACAGGGAAAGTCTTCAGATGGC AGTAGGCCCATTCCTCCACATCCTAGAGAGCCAACCTGCTGAAAGCCATGGACTCTGCCACTGC CCCCGACAAGATCAGAAAGCTGTATCTCTATGCGGCTCATGATGTGACCTTCATACCGCTCTT AATGACCCTGGGGATTTTTGACCACAAATGGCCACCGTTTGCTGTTGACCTGACCATGGAACT TTACCAGCACCTGGAATCTAAGGAGTGGTTTGTGCAGCTCTATTACCACGGGAAGGAGCAGGT GCCGAGAGGTTGCCCTGATGGGCTCTGCCCGCTGGACATGTTCTTGAATGCCATGTCAGTTTA TACCTTAAGCCCAGAAAAATACCATGCACTCTGCTCTCAAACTCAGGTGATGGAAGTTGGAAA TGAAGAG<mark>TAA</mark>CTGATTTATAAAAGCAGGATGTGTTGATTTTAAAATAAAGTGCCTTTATACAATG

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FIGURE 330

MITGVFSMRLWTPVGVLTSLAYCLHQRRVALAELQEADGQCPVDRSLLKLKMVQVVFRHGARSPLKPLPLEEQVE WNPQLLEVPPQTQFDYTVTNLAGGPKPYSPYDSQYHETTLKGGMFAGQLTKVGMQQMFALGERLRKNYVEDIPFL SPTFNPQEVFIRSTNIFRNLESTRCLLAGLFQCQKEGPIIIHTDEADSEVLYPNYQSCWSLRQRTRGRRQTASLQ PGISEDLKKVKDRMGIDSSDKVDFFILLDNVAAEQAHNLPSCPMLKRFARMIEQRAVDTSLYILPKEDRESLQMA VGPFLHILESNLLKAMDSATAPDKIRKLYLYAAHDVTFIPLLMTLGIFDHKWPPFÄVDLTMELYQHLESKEWFVQ LYYHGKEQVPRGCPDGLCPLDMFLNAMSVYTLSPEKYHALCSQTQVMEVGNEE

Important features:

Signal sequence:

amino acids 1-23

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 218-222

Casein kinase II phosphorylation site.

amino acids 87-91, 104-108, 320-324

Tyrosine kinase phosphorylation site.

amino acids 280-288

N-myristoylation site.

amino acids 15-21, 117-123, 118-124, 179-185, 240-246, 387-393

Amidation site.

amino acids 216-220

Leucine zipper pattern.

amino acids 10-32

Histidine acid phosphatases phosphohistidine signature.

amino acids 50-65

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FIGURE 331

CGAGGGCTTTTCCGGCTCCGGAATGGCACATGTGGGAATCCCAGTCTTGTTGGCTACAACATTTTTCCCTTTCCT AGCAGGGCACTCTCACTCAGGGTGACCAGCTCCTTGCCTCTCTGTGGATAACAGAGCATGAGAAAGTGAAGAGAT CCTGGAGAGCCTGGGGGGGGCCTGCCTAACAAGCTTTCAAAAAACAGGAGCGACTTCCACTGGGCTGGGATAAG TTTAACCTCTCTGGGAGATGAAAACGATGGCTTAAGGGGCCAGAAATAGAGATGCTTTGTAAAATAAAATTTTAA AAAAAGCAAGTATTTTATAGCATAAAGGCTAGAGACCAAAATAGATAACAGGATTCCCTGAACATTCCTAAGAGG GAGAAAGTATGTTAAAAATAGAAAAACCAAAATGCAGAAGGAGGAGACTCACAGAGCTAAACCAGG<u>ATG</u>GGGACC CTGGGTCAGGCCAGCCTCTTTGCTCCTCCCGGAAATTATTTTTTGGTCTGACCACTCTGCCTTGTGTTTTGCAGAA TCATGTGAGGGCCAACCGGGGAAGGTGGAGCAGATGAGCACACAGGAGCCGTCTCCTCACCGCCGCCCCTCTC AGCATGGAACAGAGGCAGCCCTGGCCCCGGGCCCTGGAGGTGGACAGCCGCTCTGTGGTCCTCTCAGTGGTC TGGGTGCTGGCCCCCCAGCAGCCGGCATGCCTCAGTTCAGCACCTTCCACTCTGAGAATCGTGACTGGACC TTCAACCACTTGACCGTCCACCAAGGGACGGGGCCGTCTATGTGGGGGCCATCAACCGGGTCTATAAGCTGACA GGCAACCTGACCATCCAGGTGGCTCATAAGACAGGGCCAGAAGAGGACAACAAGTCTCGTTACCCGCCCCTCATC GTGCAGCCCTGCAGCGAAGTGCTCACCCTCACCAACAATGTCAACAAGCTGCTCATCATTGACTACTCTGAGAAC GAGCCATCCCACAAGAAGGAGCACTACCTGTCCAGTGTCAACAAGACGGGCACCATGTACGGGGTGATTGTGCGC TCTGAGGGTGAGGATGGCAAGCTCTTCATCGGCACGCTGTGGATGGGAAGCAGGATTACTTCCCGACCCTGTCC AGCCGGAAGCTGCCCCGAGACCCTGAGTCCTCAGCCATGCTCGACTATGAGCTACACAGCGATTTTGTCTCCTCT CTCATCAAGATCCCTTCAGACACCCTGGCCCTGGTCTCCCACTTTGACATCTTCTACATCTACGGCTTTGCTAGT GGGGGCTTTGTCTACTTTCTCACTGTCCAGCCCGAGACCCCTGAGGGTGTGGCCATCAACTCCGCTGGAGACCTC TTCTACACCTCACGCATCGTGCGGCTCTGCAAGGATGACCCCAAGTTCCACTCATACGTGTCCCTGCCCTTCGGC TGCACCCGGGCCGGGTGGAATACCGCCTCCTGCAGGCTGCTTACCTGGCCAAGCCTGGGGACTCACTGGCCCAG GCCTTCAATATCACCAGCCAGGACGATGTACTCTTTGCCATCTTCTCCAAAGGGCAGAAGCAGTATCACCACCCG $\verb|CCCGATGACTCTGCCCTGTGTGCCTTCCCTATCCGGGCCATCAACTTGCAGATCAAGGAGCGCCTGCAGTCCTGC| \\$ TACCAGGCCGAGGCCAACCTGGAGCTCAACTGGCTGCTGGGGAAGGACGTCCAGTGCACGAAGGCGCCTGTCCCC ATCGATGATAACTTCTGTGGACTGGACATCAACCAGCCCCTGGGAGGCTCAACTCCAGTGGAGGGCCTGACCCTG TACACCACCAGGAGGACCGCATGACCTCTGTGGCCTCCTACGTTTACAACGGCTACAGCGTGGTTTTTGTGGGG ACTAAGAGTGGCAAGCTGAAAAAGGTAAGAGTCTATGAGTTCAGATGCTCCAATGCCATTCACCTCCTCAGCAAA ${\tt GAGTCCCTCTTGGAAGGTAGCTATTGGTGGAGATTTAACTATAGGCAACTTTATTTTCTTGGGGAACAAAGG{\color{red}{\textbf{TGA}}}$ AATGGGGAGGTAAGAAGGGGTTAATTTTGTGACTTAGCTTCTAGCTACTTCCTCCAGCCATCAGTCATTGGGTAT GTAAGGAATGCAAGCGTATTTCAATATTTCCCAAACTTTAAGAAAAACTTTAAGAAGGTACATCTGCAAAAGCAAA

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FIGURE 332

MGTLGQASLFAPPGNYFWSDHSALCFAESCEGQPGKVEQMSTHRSRLLTAAPLSMEQRQPWPR
ALEVDSRSVVLLSVVWVLLAPPAAGMPQFSTFHSENRDWTFNHLTVHQGTGAVYVGAINRVYK
LTGNLTIQVAHKTGPEEDNKSRYPPLIVQPCSEVLTLTNNVNKLLIIDYSENRLLACGSLYQG
VCKLLRLDDLFILVEPSHKKEHYLSSVNKTGTMYGVIVRSEGEDGKLFIGTAVDGKQDYFPTL
SSRKLPRDPESSAMLDYELHSDFVSSLIKIPSDTLALVSHFDIFYIYGFASGGFVYFLTVQPE
TPEGVAINSAGDLFYTSRIVRLCKDDPKFHSYVSLPFGCTRAGVEYRLLQAAYLAKPGDSLAQ
AFNITSQDDVLFAIFSKGQKQYHHPPDDSALCAFPIRAINLQIKERLQSCYQGEGNLELNWLL
GKDVQCTKAPVPIDDNFCGLDINQPLGGSTPVEGLTLYTTSRDRMTSVASYVYNGYSVVFVGT
KSGKLKKVRVYEFRCSNAIHLLSKESLLEGSYWWRFNYRQLYFLGEQR

Important features:

Signal sequence:

amino acids 1-32

Transmembrane domain:

amino acids 71-87

N-glycosylation site.

amino acids 130-134, 145-149, 217-221, 381-385

Casein kinase II phosphorylation site.

amino acids 139-143, 229-233, 240-244, 291-295, 324-328, 383-387, 384-388, 471-475, 481-485, 530-534

N-myristoylation site.

amino acids 220-226, 319-325, 353-359, 460-466, 503-509

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FIGURE 333

GCTGAGTCTGCTGCTGCTGCTGCTCCAGCCTGTAACCTGTGCCTACACCACGCCAGG CCCCCCAGAGCCCTCACCACGCTGGGCGCCCCCAGAGCCCACACCATGCCGGGCACCTACGC TCCCTCGACCACTCAGTAGTCCCAGCACCCAGGGCCTGCAAGAGCAGGCACGGGCCCTGAT GCGGGACTTCCCGCTCGTGGACGGCCACAACGACCTGCCCCTGGTCCTAAGGCAGGTTTACCA GAAAGGGCTACAGGATGTTAACCTGCGCAATTTCAGCTACGGCCAGACCAGCCTGGACAGGCT TAGAGATGGCCTCGTGGGCCCCAGTTCTGGTCAGCCTATGTGCCATGCCAGACCCAGGACCG GGATGCCCTGCGCCTCACCCTGGAGCAGATTGACCTCATACGCCGCATGTGTGCCTCCTATTC CGGTGTAGAGGGTGGCCACTCGCTGGACAATAGCCTCTCCATCTTACGTACCTTCTACATGCT GGGAGTGCGCTACCTGACGCTCACCCACACCTGCAACACCCTGGGCAGAGAGCTCCGCTAA AGAAATGAACCGCCTGGGCATGATGGTAGACTTATCCCATGTCTCAGATGCTGTGGCACGGCG GGCCCTGGAAGTGTCACAGGCACCTGTGATCTTCTCCCACTCGGCTGCCCGGGGTGTGTGCAA CAGTGCTCGGAATGTTCCTGATGACATCCTGCAGCTTCTGAAGAAGAACGGTGGCGTCGTGAT GGTGTCTTTGTCCATGGGAGTAATACAGTGCAACCCATCAGCCAATGTGTCCACTGTGGCAGA TCACTTCGACCACATCAAGGCTGTCATTGGATCCAAGTTCATCGGGATTGGTGGAGATTATGA TGGGGCCGCAAATTCCCTCAGGGGCTGGAAGACGTGTCCACATACCCGGTCCTGATAGAGGA GTTGCTGAGTCGTGGCTGGAGTGAGGAAGAGCTTCAGGGTGTCCTTCGTGGAAACCTGCTGCG GGTCTTCAGACAAGTGGAAAAGGTACAGGAAGAAAACAAATGGCAAAGCCCCTTGGAGGACAA GTTCCCGGATGAGCAGCTGAGCAGTTCCTGCCACTCCGACCTCTCACGTCTGCGTCAGAGACA GAGTCTGACTTCAGGCCAGGAACTCACTGAGATTCCCATACACTGGACAGCCAAGTTACCAGC CAAGTGGTCAGTCTCAGAGTCCTCCCCCCACATGGCCCCAGTCCTTGCAGTTGTGGCCACCTT CCCAGTCCTTATTCTGTGGCTCTGATGACCCAGTTAGTCCTGCCAGATGTCACTGTAGCAAGC **GGACATAG**

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FIGURE 334

MPGTYAPSTTLSSPSTQGLQEQARALMRDFPLVDGHNDLPLVLRQVYQKGLQDVNLRNFSYGQ
TSLDRLRDGLVGAQFWSAYVPCQTQDRDALRLTLEQIDLIRRMCASYSELELVTSAKALNDTQ
KLACLIGVEGGHSLDNSLSILRTFYMLGVRYLTLTHTCNTPWAESSAKGVHSFYNNISGLTDF
GEKVVAEMNRLGMMVDLSHVSDAVARRALEVSQAPVIFSHSAARGVCNSARNVPDDILQLLKK
NGGVVMVSLSMGVIQCNPSANVSTVADHFDHIKAVIGSKFIGIGGDYDGAGKFPQGLEDVSTY
PVLIEELLSRGWSEEELQGVLRGNLLRVFRQVEKVQEENKWQSPLEDKFPDEQLSSSCHSDLS
RLRQRQSLTSGQELTEIPIHWTAKLPAKWSVSESSPHMAPVLAVVATFPVLILWL

Important features:

N-glycosylation sites.

amino acids 58-62, 123-127, 182-186, 273-277

N-myristoylation sites.

amino acids 72-78, 133-139, 234-240, 264-270, 334-340, 389-395

Renal dipeptidase active site.

amino acids 134-157

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FIGURE 335

CCCAGAAGTTCAAGGGCCCCCGGCCTCCTGCGCTCCTGCCGCCGGGACCCTCGACCTCCTCAG AGCAGCCGGCTGCCGCCCGGGAAG<u>ATG</u>GCGAGGAGGAGCCGCCACCGCCTCCTCCTGCTGCT GCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGCCCCAAAAGA CCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAAAACCCCAAAGAA GACTGTTTCCTCCAGATTAGAGTGGAAGAAACTGGGTCGGAGTGTCTCCTTTGTCTACTATCA ACAGACTCTTCAAGGTGATTTTAAAAATCGAGCTGAGATGATAGATTTCAATATCCGGATCAA AAATGTGACAAGAAGTGATGCGGGGAAATATCGTTGTGAAGTTAGTGCCCCATCTGAGCAAGG CCAAAACCTGGAAGAGGATACAGTCACTCTGGAAGTATTAGTGGCTCCAGCAGTTCCATCATG TGAAGTACCCTCTTCTGCTCTGAGTGGAACTGTGGTAGAGCTACGATGTCAAGACAAAGAAGG GAATCCAGCTCCTGAATACACATGGTTTAAGGATGGCATCCGTTTGCTAGAAAATCCCAGACT TGGCTCCCAAAGCACCAACAGCTCATACACAATGAATACAAAAACTGGAACTCTGCAATTTAA TACTGTTTCCAAACTGGACACTGGAGAATATTCCTGTGAAGCCCGCAATTCTGTTGGATATCG CAGGTGTCCTGGGAAACGAATGCAAGTAGATGATCTCAACATAAGTGGCATCATAGCAGCCGT AGTAGTTGTGGCCTTAGTGATTTCCGTTTGTGGCCTTGGTGTATGCTCAGAGGAAAGG CTACTTTTCAAAAGAAACCTCCTTCCAGAAGAGTAATTCTTCATCTAAAGCCACGACAATGAG TGAAAATGTGCAGTGGCTCACGCCTGTAATCCCAGCACTTTGGAAGGCCGCGGCGGCGGATC ACGAGGTCAGGAGTTCTAGACCAGTCTGGCCAATATGGTGAAACCCCATCTCTACTAAAATAC AAAAATTAGCTGGGCATGGTGCCTGCCTGCAGTTCCAGCTGCTTGGGAGACAGGAGAATC ACTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCTGAGATCACGCCACTGCAGTCCAGCCTGGG TGTAGAATTCTTACAATAAATATAGCTTGATATTC

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FIGURE 336

MARRSRHRLLLLLLRYLVVALGYHKAYGFSAPKDQQVVTAVEYQEAILACKTPKKTVSSRLEW KKLGRSVSFVYYQQTLQGDFKNRAEMIDFNIRIKNVTRSDAGKYRCEVSAPSEQGQNLEEDTV TLEVLVAPAVPSCEVPSSALSGTVVELRCQDKEGNPAPEYTWFKDGIRLLENPRLGSQSTNSS YTMNTKTGTLQFNTVSKLDTGEYSCEARNSVGYRRCPGKRMQVDDLNISGIIAAVVVVALVIS VCGLGVCYAQRKGYFSKETSFQKSNSSSKATTMSENVQWLTPVIPALWKAAAGGSRGQEF

Important features:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 130-144, 238-258

N-glycosylation site.

amino acids 98-102, 187-191, 236-240, 277-281

Casein kinase II phosphorylation site.

amino acids 39-43, 59-63, 100-104, 149-153, 205-209, 284-288

N-myristoylation site.

amino acids 182-188, 239-245, 255-261, 257-263, 305-311

Amidation site.

amino acids 226-230

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FIGURE 337

GGAGCCGCCCTGGGTGTCAGCGGCTCGGCTCCCGCGCACGCTCCGGCCGTCGCGCAGCCTCGG **TG**ATTTCCCTCCGGGGCCCCTGGTGACCAACTTGCTGCGGTTTTTGTTCCTGGGGCTGAGTG CCCTCGCGCCCCCTCGCGGGCCCAGCTGCAACTGCACTTGCCCGCCAACCGGTTGCAGGCGG TGGAGGGAGGGAAGTGGTGCTTCCAGCGTGGTACACCTTGCACGGGGAGGTGTCTTCATCCC TGTCCTACATCAATGGGGTCACAACAAGCAAACCTGGAGTATCCTTGGTCTACTCCATGCCCT CCCGGAACCTGTCCCTGCGGCTGGAGGGTCTCCAGGAGAAAGACTCTGGCCCCTACAGCTGCT CCGTGAATGTGCAAGACAAACAAGGCAAATCTAGGGGCCACAGCATCAAAACCTTAGAACTCA ATGTACTGGTTCCTCCAGCTCCTCCATCCTGCCGTCTCCAGGGTGTGCCCCCATGTGGGGGCAA ACGTGACCCTGAGCTGCCAGTCTCCAAGGAGTAAGCCCGCTGTCCAATACCAGTGGGATCGGC AGCTTCCATCCTTCCAGACTTTCTTTGCACCAGCATTAGATGTCATCCGTGGGTCTTTAAGCC TCACCAACCTTTCGTCTTCCATGGCTGGAGTCTATGTCTGCAAGGCCCACAATGAGGTGGGCA CTGCCCAATGTAATGTGACGCTGGAAGTGAGCACAGGGCCTGGAGCTGCAGTGGTTGCTGGAG GGGGCAAGGCCCTGGAGGAGCCAGCCAATGATATCAAGGAGGATGCCATTGCTCCCCGGACCC TGCCCTGGCCCAAGAGCTCAGACACAATCTCCAAGAATGGGACCCTTTCCTCTGTCACCTCCG CACGAGCCCTCCGGCCACCCCATGGCCCTCCCAGGCCTGGTGCATTGACCCCCACGCCCAGTC TCTCCAGCCAGGCCCTGCCCTCACCAAGACTGCCCACGACAGATGGGGCCCACCCTCAACCAA TATCCCCCATCCCTGGTGGGGTTTCTTCCTCTGGCTTGAGCCGCATGGGTGCTGTGCCTGTGA TGGTGCCTGCCCAGAGTCAAGCTGGCTCTCTGGTATGATGACCCCACCACTCATTGGCTAAAG GATTTGGGGTCTCCTTCCTATAAGGGTCACCTCTAGCACAGAGGCCTGAGTCATGGGAAAG AGTCACACTCCTGACCCTTAGTACTCTGCCCCCACCTCTCTTTACTGTGGGAAAACCATCTCA GTAAGACCTAAGTGTCCAGGAGACAGAAGGAGAAGAGGAAGTGGATCTGGAATTGGGAGGAGC CTCCACCCACCCTGACTCCTTATGAAGCCAGCTGCTGAAATTAGCTACTCACCAAGAGT GAGGGGCAGAGACTTCCAGTCACTGAGTCTCCCAGGCCCCCTTGATCTGTACCCCACCCCTAT GTTAGGTTTTACTGGGGCAGAGGATAGGGAATCTCTTATTAAAACTAACATGAAATATGTGTT GTTTTCATTTGCAAATTTAAATAAAGATACATAATGTTTGTATGAAAAA

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FIGURE 338

MISLPGPLVTNLLRFLFLGLSALAPPSRAQLQLHLPANRLQAVEGGEVVLPAWYTLHGEVSSS QPWEVPFVMWFFKQKEKEDQVLSYINGVTTSKPGVSLVYSMPSRNLSLRLEGLQEKDSGPYSC SVNVQDKQGKSRGHSIKTLELNVLVPPAPPSCRLQGVPHVGANVTLSCQSPRSKPAVQYQWDR QLPSFQTFFAPALDVIRGSLSLTNLSSSMAGVYVCKAHNEVGTAQCNVTLEVSTGPGAAVVAG AVVGTLVGLGLLAGLVLLYHRRGKALEEPANDIKEDAIAPRTLPWPKSSDTISKNGTLSSVTS ARALRPPHGPPRPGALTPTPSLSSQALPSPRLPTTDGAHPQPISPIPGGVSSSGLSRMGAVPV MVPAQSQAGSLV

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 245-267

N-glycosylation site.

amino acids 108-112, 169-173, 213-217, 236-240, 307-311

N-myristoylation site.

amino acids 90-96, 167-173, 220-226, 231-237, 252-258, 256-262, 262-268, 308-314, 363-369, 364-370

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 164-175

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FIGURE 339

CCCTTCTC<u>ATG</u>GGACTTTGGGGACAAAGCGTCCCGACCGCCTCGAGCGCTCGAGCAGGGCGCTATCCAGGAGCCA GGACAGCGTCGGGAACCAGACCATGGCTCCTGGACCCCAAGATCCTTAAGTTCGTCGTCTTCATCGTCGCGGTTC TGCTGCCGGTCCGGGTTGACTCTGCCACCATCCCCGGCAGGACGAAGTTCCCCAGCAGACAGTGGCCCCACAGC AACAGAGGCGCAGCCTCAAGGAGGAGGAGTGTCCAGCAGGATCTCATAGATCAGAATATACTGGAGCCTGTAACC CGTGCACAGAGGGTGTGGATTACACCATTGCTTCCAACAATTTGCCTTCTTGCCTGCTATGTACAGTTTGTAAAT CAGGTCAAACAAATAAAAGTTCCTGTACCACGACCAGAGACACCGTGTGTCAGTGTGAAAAAAGGAAGCTTCCAGG ATAAAAACTCCCCTGAGATGTGCCGGACGTGTAGAACAGGGTGTCCCAGAGGGATGGTCAAGGTCAGTAATTGTA CGCCCCGGAGTGACATCAAGTGCAAAAATGAATCAGCTGCCAGTTCCACTGGGAAAACCCCAGCAGCGGAGGAGA CAGTGACCACCATCCTGGGGATGCTTGCCTCTCCCTATCACTACCTTATCATCATAGTGGTTTTAGTCATCATTTT TAGCTGTGGTTGTGGTTTGCTTTCATGTCGGAAGAAATTCATTTCTTACCTCAAAGGCATCTGCTCAGGTGGTG GAGGAGGTCCCGAACGTGTGCACAGAGTCCTTTTCCGGCGGCGTTCATGTCCTTCACGAGTTCCTGGGGCGGAGG AGGAGCTGGCAGAGCTAACAGGTGTGACTGTAGAGTCGCCAGAGGAGCCACAGCGTCTGCTGGAACAGGCAGAAG CTGAAGGGTGTCAGAGGAGGAGGCTGCTGGTTCCAGTGAATGACGCTGACTCCGCTGACATCAGCACCTTGCTGG ATGCCTCGGCAACACTGGAAGAAGGACATGCAAAGGAAACAATTCAGGACCAACTGGTGGGCTCCGAAAAGCTCT CATTTACCTTTTCTCCTACAAAGGGAAGCAGCCTGGAAGAAACAGTCCAGTACTTGACCCATGCCCCAACAAACT CTACTATCCAATATGGGGCAGCTTACCAATGGTCCTAGAACTTTGTTAACGCACTTGGAGTAATTTTTATGAAAT ACTGCGTGTGATAAGCAAACGGGAGAAATTTATATCAGATTCTTGGCTGCATAGTTATACGATTGTGTATTAAGG GTCGTTTTAGGCCACATGCGGTGGCTCATGCCTGTAATCCCAGCACTTTGATAGGCTGAGGCAGGTGGATTGCTT GAGCTCGGGAGTTTGAGACCAGCCTCATCAACACAGTGAAACTCCATCTCAATTTAAAAAGAAAAAAAGTGGTTT CTACTGGTGTGTGCATTTAATGACATCTAACTACAGATGCCGCACAGCCACAATGCTTTTGCCTTATAGTTTTTTA ACTTTAGAACGGGATTATCTTGTTATTACCTGTATTTTCAGTTTCGGATATTTTTGACTTAATGATGAGATTATC AAGACGTAGCCCTATGCTAAGTCATGAGCATATGGACTTACGAGGTTCGACTTAGAGTTTTGAGCTTTAAGATA GGATTATTGGGGCTTACCCCCACCTTAATTAGAGAAACATTTATATTGCTTACTACTGTAGGCTGTACATCTCTT TTCCGATTTTTGTATAATGATGTAAACATGGAAAAACTTTAGGAAATGCACTTATTAGGCTGTTTACATGGGTTG ATTTATAAGTAGATGTTTACATATGCCCAGGATTTTGAAGAGCCTGGTATCTTTGGGAAGCCATGTGTCTGGTTT GTCGTGCTGGGACAGTCATGGGACTGCATCTTCCGACTTGTCCACAGCAGATGAGGACAGTGAGAATTAAGTTAG ATCCGAGACTGCGAAGAGCTTCTCTTTCAAGCGCCATTACAGTTGAACGTTAGTGAATCTTGAGCCTCATTTGGG CTCAGGGCAGAGCAGGTGTTTATCTGCCCCGGCATCTGCCATGGCATCAAGAGGGAAGAGTGGACGGTGCTTGGG AATGGTGTGAAATGGTTGCCGACTCAGGCATGGATGGGCCCCTCTCGCTTCTGGTGGTCTGTGAACTGAGTCCCT CTGTAAGCATCTGACTCATCTCAGAGATATCAATTCTTAAACACTGTGACAACGGGATCTAAAAATGGCTGACACA TTTGTCCTTGTGTCACGTTCCATTATTTTATTTAAAAACCTCAGTAATCGTTTTAGCTTCTTTCCAGCAAACTCT TCTCCACAGTAGCCCAGTCGTAGGATAAATTACGGATATAGTCATTCTAGGGGTTTCAGTCTTTTCCATCTC AAGGCATTGTGTGTTTTGTTCCGGGACTGGTTTGGCTGGGACAAAGTTAGAACTGCCTGAAGTTCGCACATTCAG ATTGTTGTGTCCATGGAGTTTTAGGAGGGGATGGCCTTTCCGGTCTTCGCACTTCCATCCTCCACTTCCATC TGGCGTCCCACACCTTGTCCCCTGCACTTCTGGATGACACAGGGTGCTGCTGCCTCCTAGTCTTTGCCTTTGCTG AGAGGCCTTCCTTGAAGATGCATCTAGACTACCAGCCTTATCAGTGTTTAAGCTTATTCCTTTAACATAAGCTTC ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

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FIGURE 340

MGLWGQSVPTASSARAGRYPGARTASGTRPWLLDPKILKFVVFIVAVLLPVRVDSATIPRQDEVPQQTVAPQQQR
RSLKEEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSCLLCTVCKSGQTNKSSCTTTRDTVCQCEKGSFQDKN
SPEMCRTCRTGCPRGMVKVSNCTPRSDIKCKNESAASSTGKTPAAEETVTTILGMLASPYHYLIIIVVLVIILAV
VVVGFSCRKKFISYLKGICSGGGGGPERVHRVLFRRRSCPSRVPGAEDNARNETLSNRYLQPTQVSEQEIQGQEL
AELTGVTVESPEEPQRLLEQAEAEGCQRRRLLVPVNDADSADISTLLDASATLEEGHAKETIQDQLVGSEKLFYE
EDEAGSATSCL

Important features:

Transmembrane domains:

amino acids 35-52, 208-230

N-glycosylation sites.

amino acids 127-131, 182-186, 277-281

Glycosaminoglycan attachment site.

amino acids 245-249

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 260-264

N-myristoylation sites.

amino acids 21-27, 86-92, 102-108, 161-167, 242-248, 270-276, 297-303, 380-386

ATP/GTP-binding site motif A (P-loop).

amino acids 185-193

TNFR/NGFR cysteine-rich region.

amino acids 99-139

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FIGURE 341

GCCTCTGAATTGTTGGGCAGTCTGGCAGTGGAGCTCTCCCCGGTCTGACAGCCACTCCAGAGG CCATGCTTCGTTTCTTGCCAGATTTGGCTTTCAGCTTCCTGTTAATTCTGGCTTTGGGCCAGG CAGTCCAATTTCAAGAATATGTCTTTCTCCAATTTCTGGGCTTAGATAAGGCGCCTTCACCCC AGAAGTTCCAACCTGTGCCTTATATCTTGAAGAAAATTTTCCAGGATCGCGAGGCAGCAGCA CCACTGGGGTCTCCCGAGACTTATGCTACGTAAAGGAGCTGGGCGTCCGCGGGAATGTACTTC GCTTTCTCCCAGACCAAGGTTTCTTTCTTTACCCAAAGAAAATTTCCCAAGCTTCCTCCTGCC AGCTGGGCCTGGACTTGGGGCCCAATTCTTACTATAACCTGGGACCAGAGCTGGAACTGGCTC TGTTCCTGGTTCAGGAGCCTCATGTGTGGGGCCAGACCACCCCTAAGCCAGGTAAAATGTTTG TGTTGCGGTCAGTCCCATGGCCACAAGGTGCTGTTCACCTTCAACCTGCTGGATGTAGCTAAGG ATTGGAATGACAACCCCCGGAAAAATTTCGGGTTATTCCTGGAGATACTGGTCAAAGAAGATA GAGACTCAGGGGTGAATTTTCAGCCTGAAGACACCTGTGCCAGACTAAGATGCTCCCTTCATG CTTCCCTGCTGGTGGTGACTCTCAACCCTGATCAGTGCCACCCTTCTCGGAAAAGGAGAGCAG CCATCCCTGTCCCCAAGCTTTCTTGTAAGAACCTCTGCCACCGTCACCAGCTATTCATTAACT TCCGGGACCTGGGTTGGCACAAGTGGATCATTGCCCCCAAGGGGTTCATGGCAAATTACTGCC ATGGAGAGTGTCCCTTCTCACTGACCATCTCTCTCAACAGCTCCAATTATGCTTTCATGCAAG CCCTGATGCATGCCGTTGACCCAGAGATCCCCCAGGCTGTGTGTATCCCCACCAAGCTGTCTC CCATTTCCATGCTCTACCAGGACAATAATGACAATGTCATTCTACGACATTATGAAGACATGG TAGTCGATGAATGTGGGTGTGGG**TAG**GATGTCAGAAATGGGAATAGAAGGAGTGTTCTTAGGG TAAATCTTTTAATAAAACTACCTATCTGGTTTATGACCACTTAGATCGAAATGTC

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FIGURE 342

MLRFLPDLAFSFLLILALGQAVQFQEYVFLQFLGLDKAPSPQKFQPVPYILKKIFQDREAAAT
TGVSRDLCYVKELGVRGNVLRFLPDQGFFLYPKKISQASSCLQKLLYFNLSAIKEREQLTLAQ
LGLDLGPNSYYNLGPELELALFLVQEPHVWGQTTPKPGKMFVLRSVPWPQGAVHFNLLDVAKD
WNDNPRKNFGLFLEILVKEDRDSGVNFQPEDTCARLRCSLHASLLVVTLNPDQCHPSRKRRAA
IPVPKLSCKNLCHRHQLFINFRDLGWHKWIIAPKGFMANYCHGECPFSLTISLNSSNYAFMQA
LMHAVDPEIPQAVCIPTKLSPISMLYQDNNDNVILRHYEDMVVDECGCG

Important features:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 112-116, 306-310

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 96-100

N-myristoylation site.

amino acids 77-83

TGF-beta family proteins.

amino acids 264-299, 327-341, 345-364

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FIGURE 343

TTTTTTCCATCTCTGGGCCAGCTTGGGATCCTAGGCCGCCCTGGGAAGACATTTGTGTTTTTACACACATAAGGAT GCTCAGTGCTTGCACTTATCTGCCTAGGTACATCGAAGTCTTTTGACCTCCATACAGTGATTATGCCTGTC ATCGCTGGTGGTATCCTGGCGGCCTTGCTCCTGCTGATAGTTGTCGTGCTCTTTACTTCAAAATACACAAC AACAGCCAGGCCAAAACCATTGCCACGGAGTCTTGTCCTGCCCTGCAGTGCTGAAGGATATAGAATGTGTGCC AGTTTTGATTCCCTGCCACCTTGCTGTTGCGACATAAATGAGGGCCTCTGAGTTAGGAAAGGCTCCCTTCTCAAA GCAGAGCCCTGAAGACTTCAATGATGTCAATGAGGCCACCTGTTTGTGATGTGCAGGCACAGAAGAAAAGGCACAG CTCCCCATCAGTTCATGGAAAATAACTCAGTGCCTGCTGGGAACCAGCTGCTGGAGATCCCTACAGAGAGCTTC CACTGGGGGCAACCCTTCCAGGAAGGAGTTGGGGGAGAGAGCCCTCACTGTGGGGAATGCTGATAAACCAGTCA CACAGCTGCTCTATTCTCACACAAATCTACCCCTTGCGTGGCTGGAACTGACGTTTCCCTGGAGGTGTCCAGAAA GCTGATGTAACACAGAGCCTATAAAAGCTGTCGGTCCTTAAGGCTGCCCAGCGCCTTGCCAAA**ATG**GAGCTTGTA AGAAGGCTCATGCCATTGACCCTCTTAATTCTCTCCTGTTTGGCGGAGCTGACAATGGCGGAGGCTGAAGGCAAT GCAAGCTGCACAGTCAGTCTAGGGGGTGCCAATATGGCAGAGACCCACAAAGCCATGATCCTGCAACTCAATCCC AGTGAGAACTGCACCTGGACAATAGAAAGACCAGAAAACAAAAGCATCAGAATTATCTTTTCCTATGTCCAGCTT GATCCAGATGGAAGCTGTGAAAGTGAAAACATTAAAGTCTTTGACGGAACCTCCAGCAATGGGCCTCTGCTAGGG CAAGTCTGCAGTAAAAACGACTATGTTCCTGTATTTGAATCATCATCCAGTACATTGACGTTTCAAATAGTTACT GACTCAGCAAGAATTCAAAGAACTGTCTTTGTCTTCTACTACTTCTTCTCTCTAACATCTCTATTCCAAACTGT GGCGGTTACCTGGATACCTTGGAAGGATCCTTCACCAGCCCCAATTACCCAAAGCCGCATCCTGAGCTGGCTTAT TGTGTGTGGCACATACAAGTGGAGAAAGATTACAAGATAAAACTTAAACTTCAAAGAGATTTTCCTAGAAATAGAC AAACAGTGCAAATTTGATTTCTTGCCATCTATGATGGCCCCTCCACCAACTCTGGCCTGATTGGACAAGTCTGT GGCCGTGTGACTCCCACCTTCGAATCGTCATCAAACTCTCTGACTGTCGTGTTGTCTACAGATTATGCCAATTCT ${\tt TACCGGGGATTTTCTGCTTCCTACACCTCAATTTATGCAGAAAACATCAACACTACATCTTTAACTTGCTCTTCT}$ GACAGGATGAGAGTTATTATAAGCAAATCCTACCTAGAGGCTTTTAACTCTAATGGGAATAACTTGCAACTAAAA GACCCAACTTGCAGACCAAAATTATCAAATGTTGTGGAATTTTCTGTCCCTCTTAATGGATGTGGTACAATCAGA AAGGTAGAAGATCAGTCAATTACTTACACCAATATAATCACCTTTTCTGCATCCTCAACTTCTGAAGTGATCACC CGTCAGAAACAACTCCAGATTATTGTGAAGTGTGAAATGGGACATAATTCTACAGTGGAGATAATATACATAACA GAAGATGATGTAATACAAAGTCAAAATGCACTGGGCAAATATAACACCAGCATGGCTCTTTTTGAATCCAATTCA TTTGAAAAGACTATACTTGAATCACCATATTATGTGGATTTGAACCAAACTCTTTTTGTTCAAGTTAGTCTGCAC ACCTCAGATCCAAATTTGGTGGTGTTTCTTGATACCTGTAGAGCCTCTCCCACCTCTGACTTTGCATCTCCAACC TACGACCTAATCAAGAGTGGATGTAGTCGAGATGAAACTTGTAAGGTGTATCCCTTATTTGGACACTATGGGAGA TTCCAGTTTAATGCCTTTAAATTCTTGAGAAGTATGAGCTCTGTGTATCTGCAGTGTAAAGTTTTGATATGTGAT AGCAGTGACCACCAGTCTCGCTGCAATCAAGGTTGTGTCTCCAGAAGCAAACGAGACATTTCTTCATATAAATGG AAAACAGATTCCATCATAGGACCCATTCGTCTGAAAAGGGATCGAAGTGCAAGTGGCAATTCAGGATTTCAGCAT GAAACACATGCGGAAGAAACTCCAAACCAGCCTTTCAACAGTGTGCATCTGTTTTCCTTCATGGTTCTAGCTCTG AATGTGGTGACTGTAGCGACAATCACAGTGAGGCATTTTGTAAATCAACGGGCAGACTACAAATACCAGAAGCTG ${\tt CAGAACTAT} \underline{\textbf{TAA}} {\tt CTAACAGGTCCAACCCTAAGTGAGACATGTTTCTCCAGGATGCCAAAGGAAATGCTACCTCGT}$ GGCTACACATATTATGAATAAATGAGGAAGGGCCTGAAAGTGACACACAGGCCTGCATGTAAAAAAA

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FIGURE 344

MELVRRLMPLTLLILSCLAELTMAEAEGNASCTVSLGGANMAETHKAMILQLNPSENCTWTIE
RPENKSIRIIFSYVQLDPDGSCESENIKVFDGTSSNGPLLGQVCSKNDYVPVFESSSSTLTFQ
IVTDSARIQRTVFVFYYFFSPNISIPNCGGYLDTLEGSFTSPNYPKPHPELAYCVWHIQVEKD
YKIKLNFKEIFLEIDKQCKFDFLAIYDGPSTNSGLIGQVCGRVTPTFESSSNSLTVVLSTDYA
NSYRGFSASYTSIYAENINTTSLTCSSDRMRVIISKSYLEAFNSNGNNLQLKDPTCRPKLSNV
VEFSVPLNGCGTIRKVEDQSITYTNIITFSASSTSEVITRQKQLQIIVKCEMGHNSTVEIIYI
TEDDVIQSQNALGKYNTSMALFESNSFEKTILESPYYVDLNQTLFVQVSLHTSDPNLVVFLDT
CRASPTSDFASPTYDLIKSGCSRDETCKVYPLFGHYGRFQFNAFKFLRSMSSVYLQCKVLICD
SSDHQSRCNQGCVSRSKRDISSYKWKTDSIIGPIRLKRDRSASGNSGFQHETHAEETPNQPFN
SVHLFSFMVLALNVVTVATITVRHFVNQRADYKYQKLQNY

Important features:

Signal sequence:

amino acids 1-24

Transmembrane domain:

amino acids 571-586

N-glycosylation site.

amino acids 29-33, 57-61, 67-71, 148-152, 271-275, 370-374, 394-398, 419-423

Casein kinase II phosphorylation site.

amino acids 22-26, 108-112, 289-293, 348-352, 371-375, 379-383, 408-412, 463-467, 520-524, 556-560

Tyrosine kinase phosphorylation site.

amino acids 172-180, 407-415, 407-416, 519-528

N-myristoylation site.

amino acids 28-34, 38-44, 83-89, 95-101, 104-110, 226-232

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 7-18

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FIGURE 345

TGGGGGCCCCCAGGCTCGCGCGTGGAGCGAAGCAGCATGGGCAGTCGGTGCGCGCTGGCCCTGGCGGTGCTCTC GGCCTTGCTGTGTCAGGTCTGGAGCTCTGGGGTGTTCGAACTGAAGCTGCAGGAGTTCGTCAACAAGAAGGGGGCT GCTGGGGAACCGCAATTGCTGCCGCGGGGGCCCGGGGCCACCGCCGTGCGCCTGCCGGACCTTCTTCCGCGTGTG CGTCGACTCCTTCAGTCTGCCCGACGGCGGGGGGCGCCGACTCCGCGTTCAGCAACCCCATCCGCTTCCCCTTCGG CTTCACCTGGCCGGCCACCTTCTCTCTGATTATTGAAGCTCTCCACACAGATTCTCCTGATGACCTCGCAACAGA GCACAGCAGCGCCCCACGGACCTCAAGTACTCCTACCGCTTCGTGTGTGACGAACACTACTACGGAGAGGGCTG CTCCGTTTTCTGCCGTCCCCGGGACGATGCCTTCGGCCACTTCACCTGTGGGGAGCGTGGGGAGAAAGTGTGCAA CAAACCAGGGGAATGCAAGTGCAGAGTGGGCTGGCAGGGCCGGTACTGTGACGAGTGTATCCGCTATCCAGGCTG TCTCCATGGCACCTGCCAGCAGCCCTGGCAGTGCAACTGCCAGGAAGGCTGGGGGGGCCTTTTCTGCAACCAGGA CCTGAACTACTGCACACCATAAGCCCTGCAAGAATGGAGCCACCTGCACCAACACGGGCCAGGGGAGCTACAC TTGCTCTTGCCGGCCTGGGTACACAGGTGCCACCTGCGAGCTGGGGATTGACGAGTGTGACCCCAGCCCTTGTAA GAACGGAGGGAGCTGCACGGATCTCGAGAACAGCTACTCCTGTACCTGCCCACCCGGCTTCTACGGCAAAATCTG TGAATTGAGTGCCATGACCTGTGCGGACGGCCCTTGCTTTAACGGGGGTCGGTGCTCAGACAGCCCCGATGGAGG GTACAGCTGCCGCTGCCCGTGGGCTACTCCGGCTTCAACTGTGAGAAAAATTGACTACTGCAGCTCTTCACC CTGTTCTAATGGTGCCAAGTGTGTGGACCTCGGTGATGCCTACCTGTGCCGCTGCCAGGCCGGCTTCTCGGGGAG GCACTGTGACGACAACGTGGACGACTGCGCCTCCCCGTGCGCCAACGGGGGCACCTGCCGGGATGGCGTGAA CGACTTCTCCTGCACCTGCCCGCCTGGCTACACGGGCAGGAACTGCAGTGCCCCCGTCAGCAGGTGCGAGCACGC ACCCTGCCACAATGGGGCCACCTGCCACGAGAGGGGCCACCGCTATGTGTGCGAGTGTGCCCGAGGCTACGGGGG TCCCAACTGCCAGTTCCTGCTCCCCGAGCTGCCCCCGGGCCCAGCGGTGGTGGACCTCACTGAGAAGCTAGAGGG CCAGGGCGGCCATTCCCCTGGGTGGCCGTGTGCGCCGGGGTCATCCTTGTCCTCATGCTGCTGCTGGGCTGTGC CGCTGTGGTGGTCTGCGTCCGGCTGAGGCTGCAGAAGCACCGGCCCCCAGCCGACCCCTGCCGGGGGGAGACGGA GAACACCAACAAGAAGGCGGACTTCCACGGGGACCACAGCGCCGACAAGAATGGCTTCAAGGCCCGCTACCCAGC GGTGGACTATAACCTCGTGCAGGACCTCAAGGGTGACGACACCGCCGTCAGGGACGCGCACAGCAAGCGTGACAC CAAGTGCCAGCCCCAGGGCTCCTCAGGGGAGAGAGGGGACCCCGACCACTCAGGGGTGGAGAAGCATCTGA AAGAAAAAGGCCGGACTCGGGCTGTTCAACTTCAAAAGACACCAAGTACCAGTCGGTGTACGTCATATCCGAGGA ${\tt GAAGGATGAGTGCGTCATAGCAACTGAGGTG} \underline{{\tt TAA}} {\tt AATGGAAGTGAGATGGCAAGACTCCCGTTTCTCTTAAAATA}$ ACCGAGTTCAGACCGAGCAGGTTCTCCTCCTGAGGTCCTCGACGCCTGCCGACAGCCTGTCGCGGCCCGGCCGCC GAACTGAATTACGCATAAGAAGCATGCACTGCCTGAGTGTATATTTTTGGATTCTTATGAGCCAGTCTTTTCTTGA ATTAGAAACACAAACACTGCCTTTATTGTCCTTTTTGATACGAAGATGTGCTTTTTCTAGATGGAAAAGATGTGT GTTATTTTTGGATTTGTAAAAATATTTTTCATGATATCTGTAAAGCTTGAGTATTTTGTGATGTTCGTTTTTTA TTATGGAATATTGTGCAAATGTTATTTGAGTTTTTTACTGTTTTGTTAATGAAGAAATTCCTTTTTAAAATATTT AAAAAAA

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FIGURE 346

MGSRCALALAVLSALLCQVWSSGVFELKLQEFVNKKGLLGNRNCCRGGAGPPPCACRTFFRVC LKHYQASVSPEPPCTYGSAVTPVLGVDSFSLPDGGGADSAFSNPIRFPFGFTWPGTFSLIIEA LHTDSPDDLATENPERLISRLATQRHLTVGEEWSQDLHSSGRTDLKYSYRFVCDEHYYGEGCS VFCRPRDDAFGHFTCGERGEKVCNPGWKGPYCTEPICLPGCDEQHGFCDKPGECKCRVGWQGR YCDECIRYPGCLHGTCQQPWQCNCQEGWGGLFCNQDLNYCTHHKPCKNGATCTNTGQGSYTCS CRPGYTGATCELGIDECDPSPCKNGGSCTDLENSYSCTCPPGFYGKICELSAMTCADGPCFNG GRCSDSPDGGYSCRCPVGYSGFNCEKKIDYCSSSPCSNGAKCVDLGDAYLCRCQAGFSGRHCD DNVDDCASSPCANGGTCRDGVNDFSCTCPPGYTGRNCSAPVSRCEHAPCHNGATCHERGHRYV CECARGYGGPNCQFLLPELPPGPAVVDLTEKLEGQGGPFPWVAVCAGVILVLMLLLGCAAVVV CVRLRLQKHRPPADPCRGETETMNNLANCQREKDISVSIIGATQIKNTNKKADFHGDHSADKN GFKARYPAVDYNLVQDLKGDDTAVRDAHSKRDTKCQPQGSSGEEKGTPTTLRGGEASERKRPD SGCSTSKDTKYQSVYVISEEKDECVIATEV

Important features:

Signal sequence:

Amino acids 1-21

Transmembrane domain:

Amino acids 546-566

N-glycosylation site:

Amino acids 477-481

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 660-664

Tyrosine kinase phosphorylation sites:

Amino acids 176-185;252-261

N-myristoylation sites:

Amino acids 2-8;37-43;40-46;98-104;99-105;262-268;281-287; 282-288;301-307;310-316;328-334;340-344;378-384;387-393;512-518; 676-682;683-689;695-701

Aspartic acid and asparagine hydroxylation sites:

Amino acids 343-355;420-432;458-470

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 552-563

EGF-like domain cysteine pattern signature:

Amino acids 243-255;274-286;314-326;352-364;391-403;429-441;467-479;505-517

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FIGURE 347

CCCACGCGTCCGCACCTCGGCCCCGGGCTCCGAAGCGGCTCGGGGGCGCCCTTTCGGTCAACA GGAGCCGGCCGGAAGCGCG**ATG**GGGGCCCCAGCCGCCTCGCTCCTGCTCCTGCTGCTGT CTGATGAAACAGTGGTGGCTGGTGGCACCGTGGTGCTCAAGTGCCAAGTGAAAGATCACGAGG ACTCATCCCTGCAATGGTCTAACCCTGCTCAGCAGACTCTCTACTTTGGGGAGAAGAGACCC TTCGAGATAATCGAATTCAGCTGGTTACCTCTACGCCCCACGAGCTCAGCATCAGCATCAGCA ATGTGGCCCTGGCAGACGAGGGCGAGTACACCTGCTCAATCTTCACTATGCCTGTGCGAACTG CCAAGTCCCTCGTCACTGTGCTAGGAATTCCACAGAAGCCCATCATCACTGGTTATAAATCTT CATTACGGGAAAAAGACACAGCCACCCTAAACTGTCAGTCTTCTGGGAGCAAGCCTGCAGCCC CCAATGGTAAAACCTTCACTGTCAGCAGCTCGGTGACATTCCAGGTTACCCGGGAGGATGATG GGGCGAGCATCGTGTGCTCTGTGAACCATGAATCTCTAAAGGGAGCTGACAGATCCACCTCTC AACGCATTGAAGTTTTATACACACCAACTGCGATGATTAGGCCAGACCCTCCCCATCCTCGTG AGGGCCAGAAGCTGTTGCTACACTGTGAGGGTCGCGGCAATCCAGTCCCCCAGCAGTACCTAT GGGAGAAGGAGGCAGTGTGCCACCCCTGAAGATGACCCAGGAGAGTGCCCTGATCTTCCCTT TCCTCAACAAGAGTGACAGTGGCACCTACGGCTGCACAGCCACCAGCAACATGGGCAGCTACA AGGCCTACTACACCCTCAATGTTAATGACCCCAGTCCGGTGCCCTCCTCCTCCAGCACCTACC ACGCCATCATCGGTGGGATCGTGGCTTTCATTGTCTTCCTGCTGCTCATCATGCTCATCTTCC TTGGCCACTACTTGATCCGGCACAAAGGAACCTACCTGACACATGAGGCAAAAGGCTCCGACG ATGCTCCAGACGCGGACACGCCATCATCAATGCAGAAGGCGGGCAGTCAGGAGGGGACGACA AGAAGGAATATTTCATC**TAG**AGGCGCCTGCCCACTTCCTGCGCCCCCCAGGGGCCCTGTGGGG ACTGCTGGGGCCGTCACCAACCCGGACTTGTACAGAGCAACCGCAGGGCCGCCCCTCCCGCTT GCTCCCCAGCCCACCCCCCTGTACAGAATGTCTGCTTTGGGTGCGGTTTTGTACTCGGT TTGGAATGGGGAGGGGGGGGGGGGGGGGGGGGTTGCCCTCAGCCCTTTCCGTGGCTT CTCTGCATTTGGGTTATTATTATTTTTGTAACAATCCCAAATCAAATCTGTCTCCAGGCTGGA

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FIGURE 348

MGAPAASLLLLLLLFACCWAPGGANLSQDDSQPWTSDETVVAGGTVVLKCQVKDHEDSSLQWS
NPAQQTLYFGEKRALRDNRIQLVTSTPHELSISISNVALADEGEYTCSIFTMPVRTAKSLVTV
LGIPQKPIITGYKSSLREKDTATLNCQSSGSKPAARLTWRKGDQELHGEPTRIQEDPNGKTFT
VSSSVTFQVTREDDGASIVCSVNHESLKGADRSTSQRIEVLYTPTAMIRPDPPHPREGQKLLL
HCEGRGNPVPQQYLWEKEGSVPPLKMTQESALIFPFLNKSDSGTYGCTATSNMGSYKAYYTLN
VNDPSPVPSSSSTYHAIIGGIVAFIVFLLLIMLIFLGHYLIRHKGTYLTHEAKGSDDAPDADT
AIINAEGGQSGGDDKKEYFI

Important features:

Signal sequence:

amino acids 1-20

Transmembrane domain:

amino acids 331-352

N-glycosylation site.

amino acids 25-29, 290-294

Casein kinase II phosphorylation site.

amino acids 27-31, 35-39, 89-93, 141-145, 199-203, 388-392

N-myristoylation site.

amino acids 2-8, 23-29, 156-162, 218-224, 295-301, 298-304, 306-310, 334-340, 360-364, 385-389, 386-390

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 7-18

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FIGURE 349

ACTTGCCATCACCTGTTGCCAGTGTGGAAAAATTCTCCCTGTTGAATTTTTTGCACATGGAGGACAGCAAAG AGGGCAACACAGGCTGATAAGACCAGAGACAGCAGGGGGGGAGATTATTTTACCATACGCCCTCAGGACGTTCCCTCTA $\tt TTTCCCACCACATTGTATTTATTTCCGTACTTCAGAA{\color{red}{\textbf{ATG}}} GGCCTACAGACCACAAAGTGGCCCAGCCATGGGG$ CTTTTTTCCTGAAGTCTTGGCTTATCATTTCCCTGGGGCTCTACTCACAGGTGTCCAAACTCCTGGCCTGCCCTA GTGTGTGCCGCTGCGACAGGAACTTTGTCTACTGTAATGAGCGAAGCTTGACCTCAGTGCCTCTTGGGATCCCGG AGGGCGTAACCGTACTCTACCTCCACAACAACCAAATTAATAATGCTGGATTTCCTGCAGAACTGCACAATGTAC AGTCGGTGCACACGGTCTACCTGTATGGCAACCAACTGGACGAATTCCCCATGAACCTTCCCAAGAATGTCAGAG TTCTCCATTTGCAGGAAAACAATATTCAGACCATTTCACGGGCTGCTCTTGCCCAGCTCTTGAAGCTTGAAGAGC TGCACCTGGATGACAACTCCATATCCACAGTGGGGGTGGAAGACGGGGCCTTCCGGGAGGCTATTAGCCTCAAAT TGTTGTTTTTGTCTAAGAATCACCTGAGCAGTGTGCCTGTTGGGCTTCCTGTGGACTTGCAAGAGCTGAGAGTGG ATGAAAATCGAATTGCTGTCATATCCGACATGGCCTTCCAGAATCTCACGAGCTTGGAGCGTCTTATTGTGGACG GGAACCTCCTGACCAACAAGGGTATCGCCGAGGGCACCTTCAGCCATCTCACCAAGCTCAAGGAATTTTCAATTG TACGTAATTCGCTGTCCCACCTCCTCCCGATCTCCCAGGTACGCATCTGATCAGGCTCTATTTGCAGGACAACC TGCGGATGCTGACTCAAGGGGTTTTTGATAATCTCTCCAACCTGAAGCAGCTCACTGCTCGGAATAACCCTTGGT TTTGTGACTGCAGTATTAAATGGGTCACAGAATGGCTCAAATATATCCCTTCATCTCTCAACGTGCGGGGTTTCA TGTGCCAAGGTCCTGAACAAGTCCGGGGGATGGCCGTCAGGGAATTAAATATGAATCTTTTGTCCTGTCCCACCA CGACCCCGGCCTGCCTCTCTCACCCCAGCCCCAAGTACAGCTTCTCCGACCACTCAGCCTCCCACCCTCTCTA TTCCAAACCCTAGCAGAAGCTACACGCCTCCAACTCCTACCACATCGAAACTTCCCACGATTCCTGACTGGGATG GCAGAGAAAGAGTGACCCCACCTATTTCTGAACGGATCCAGCTCTCTATCCATTTTGTGAATGATACTTCCATTC AAGTCAGCTGGCTCTCTCTCTCACCGTGATGGCATACAAACTCACATGGGTGAAAATGGGCCACAGTTTAGTAG GGGGCATCGTTCAGGAGCGCATAGTCAGCGGTGAGAAGCAACACCTGAGCCTGGTTAACTTAGAGCCCCGATCCA CCTATCGGATTTGTTTAGTGCCACTGGATGCTTTTAACTACCGCGCGGTAGAAGACACCATTTGTTCAGAGGCCA CCACCCATGCCTCCTATCTGAACAACGGCAGCACCACGCGTCCAGCCATGAGCAGACGACGTCCCACAGCATGG GCTCCCCTTTCTGCTGGCGGGCTTGATCGGGGGCGCGTGATATTTGTGCTGGTGGTCTTGCTCAGCGTCTTTT GCTGGCATATGCACAAAAAGGGGCGCTACACCTCCCAGAAGTGGAAATACAACCGGGGCCGGGAAAGATGATT ATTGCGAGGCAGGCACCAAGAAGGACACTCCATCCTGGAGATGACAGAAACCAGTTTTCAGATCGTCTCCTTAA ACTGCCATATCCCCAACAACATGCGATACTGCAACAGCAGCGTGCCAGACCTGGAGCACTGCCATACG<u>TGA</u>CAGC CAGAGGCCCAGCGTTATCAAGGCGGACAATTAGACTCTTGAGAACACTCGTGTGTGCACATAAAGACACGCAG ATTACATTTGATAAATGTTACACAGATGCATTTGTGCATTTGAATACTCTGTAATTTATACGGTGTACTATATAA TGGGATTTAAAAAAGTGCTATCTTTTCTATTTCAAGTTAATTACAAACAGTTTTTGTAACTCTTTGCTTTTTAAA TCTT

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FIGURE 350

MGLQTTKWPSHGAFFLKSWLIISLGLYSQVSKLLACPSVCRCDRNFVYCNERSLTSVPLGIPE GVTVLYLHNNQINNAGFPAELHNVQSVHTVYLYGNQLDEFPMNLPKNVRVLHLQENNIQTISR AALAQLLKLEELHLDDNSISTVGVEDGAFREAISLKLLFLSKNHLSSVPVGLPVDLQELRVDE NRIAVISDMAFQNLTSLERLIVDGNLLTNKGIAEGTFSHLTKLKEFSIVRNSLSHPPPDLPGT HLIRLYLQDNQINHIPLTAFSNLRKLERLDISNNQLRMLTQGVFDNLSNLKQLTARNNPWFCD CSIKWVTEWLKYIPSSLNVRGFMCQGPEQVRGMAVRELNMNLLSCPTTTPGLPLFTPAPSTAS PTTQPPTLSIPNPSRSYTPPTPTTSKLPTIPDWDGRERVTPPISERIQLSIHFVNDTSIQVSW LSLFTVMAYKLTWVKMGHSLVGGIVQERIVSGEKQHLSLVNLEPRSTYRICLVPLDAFNYRAV EDTICSEATTHASYLNNGSNTASSHEQTTSHSMGSPFLLAGLIGGAVIFVLVVLLSVFCWHMH KKGRYTSQKWKYNRGRRKDDYCEAGTKKDNSILEMTETSFQIVSLNNDQLLKGDFRLQPIYTP NGGINYTDCHIPNNMRYCNSSVPDLEHCHT

Important features:

Signal peptide:

amino acids 1-42

Transmembrane domain:

amino acids 542-561

N-glycosylation site.

amino acids 202-206, 298-302, 433-437, 521-525, 635-639, 649-653

Casein kinase II phosphorylation site.

amino acids 204-208, 407-411, 527-531, 593-597, 598-602, 651-655

Tyrosine kinase phosphorylation site.

amino acids 319-328

N-myristoylation site.

amino acids 2-8, 60-66, 149-155, 213-219, 220-226, 294-300, 522-528, 545-551, 633-639

Amidation site.

amino acids 581-585

Leucine zipper pattern.

amino acids 164-186

Phospholipase A2 aspartic acid active site.

amino acids 39-50

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FIGURE 351

AGCCGACGCTGCTCAAGCTGCAACTCTGTTGCAGTTGGCAGTTCTTTTCGGTTTCCCTCCTGCTGTTTTGGGGGCCA GCGGTGCTGGGCCGCTGGCCGGTCCGACAGCGGCGGTCGCGGGAACTCGGGCAGCCCTCTGGGGTAGCCGCC GAGCGCCCATGCCCCACTACCTGCCGCTGCCTCGGGGACCTGCTGGACTGCAGTCGTAAGCGGCTAGCGCGTCTT CCCGAGCCACTCCCGTCCTGGGTCGCTCGGCTGGACTTAAGTCACAACAGATTATCTTTCATCAAGGCAAGTTCC ATGAGCCACCTTCAAAGCCTTCGAGAAGTGAAACTGAACAACAATGAATTGGAGACCATTCCAAATCTGGGACCA GTCTCGGCAAATATTACACTTCTCCTTGGCTGGAAACAGGATTGTTGAAATACTCCCTGAACATCTGAAAGAG TTTCAGTCCCTTGAAACTTTGGACCTTAGCAGCAACAATATTTCAGAGCTCCAAACTGCATTTCCAGCCCTACAG CTCAAATATCTGTATCTCAACAGCAACCGAGTCACATCAATGGAACCTGGGTATTTTGACAATTTGGCCAACACA CATCTCGAATTGAACCGAAACAAGATTAAAAATGTAGATGGACTGACATTCCAAGGCCTTGGTGCTCTGAAGTCT CTCAGCCAAAATGCCATCAACAGGATCAGCCCTGATGCCTGGGAGTTCTGCCAGAAGCTCAGTGAGCTGGACCTA ACTTTCAATCACTTATCAAGGTTAGATGATTCAAGCTTCCTTGGCCTAAGCTTACTAAATACACTGCACATTGGG AACAACAGAGTCAGCTACATTGCTGATTGTGCCTTCCGGGGGCTTTCCAGTTTAAAGACTTTGGATCTGAAGAAC AATGAAATTTCCTGGACTATTGAAGACATGAATGGTGCTTTCTCTGGGCTTGACAAACTGAGGCGACTGATACTC CAAGGAAATCGGATCCGTTCTATTACTAAAAAAGCCTTCACTGGTTTGGATGCATTGGAGCATCTAGACCTGAGT GACAACGCAATCATGTCTTTACAAGGCAATGCATTTTCACAAATGAAGAAACTGCAACAATTGCATTTAAATACA AATGCCAGTTGTGCCCATCCTCAGCTGCTAAAAGGAAGAAGCATTTTTGCTGTTAGCCCAGATGGCTTTGTGTGT GATGATTTTCCCAAACCCCAGATCACGGTTCAGCCAGAAACACAGTCGGCAATAAAAGGTTCCAATTTGAGTTTC ATCTGCTCAGCTGCCAGCAGCAGTGATTCCCCCAATGACTTTTGCTTGGAAAAAAAGACAATGAACTACTGCATGAT GCTGAAATGGAAAATTATGCACACCTCCGGGCCCAAGGTGGCGAGGTGATGGAGTATACCACCATCCTTCGGCTG CGCGAGGTGGAATTTGCCAGTGAGGGGAAATATCAGTGTGTCATCTCCAATCACTTTGGTTCATCCTACTCTGTC AAAGCCAAGCTTACAGTAAATATGCTTCCCTCATTCACCAAGACCCCCATGGATCTCACCATCCGAGCTGGGGCC ATGCACGCTTGGAGTGTGCTGCTGTGGGGCACCCAGCCCCCCAGATAGCCTGGCAGAAGGATGGGGGCACAGAC TTCCCAGCTGCACGGGAGACGCATGCATGTGATGCCCGAGGATGACGTGTTCTTTATCGTGGATGTGAAGATA GAGGACATTGGGGTATACAGCTGCACAGCTCAGAACAGTGCAGGAAGTATTTCAGCAAATGCAACTCTGACTGTC CTAGAAACACCATCATTTTTGCGGCCACTGTTGGACCGAACTGTAACCAAGGGAGAAACAGCCGTCCTACAGTGC ATTGCTGGAGGAAGCCCTCCCCTAAACTGAACTGGACCAAAGATGATAGCCCATTGGTGGTAACCGAGAGGCAC TTTTTTGCAGCAGCCAATCAGCTTCTGATTATTGTGGACTCAGATGTCAGTGATGCTGGGAAATACACATGTGAG ${\tt ATGTCTAACACCCTTGGCACTGAGAGAGGAAACGTGCGCCTCAGTGTGATCCCCACCTCCAACCTGCGACTCCCCT}$ CAGATGACAGCCCCATCGTTAGACGATGACGGATGGGCCACTGTGGGTGTCGTGATCATAGCCGTGGTTTGCTGT GTGGTGGCACGTCACTCGTGTGGGTGGTCATCATATACCACACAAGGCGGAGGAATGAAGATTGCAGCATTACC **AACACAGATGAGACCAACTTGCCAGCAGATATTCCTAGTTATTTGTCATCTCAGGGAACGTTAGCTGACAGGCAG** GATGGGTACGTGTCTTCAGAAAGTGGAAGCCACCACCAGTTTGTCACATCTTCAGGTGCTGGATTTTTCTTACCA CAACATGACAGTAGTGGGACCTGCCATATTGACAATAGCAGTGAAGCTGATGTGGAAGCTGCCACAGATCTGTTC CTTTGTCCGTTTTTGGGATCCACAGGCCCTATGTATTTGAAGGGAAATGTGTATGGCTCAGATCCTTTTGAAACA TATCATACAGGTTGCAGTCCTGACCCAAGAACAGTTTTAATGGACCACTATGAGCCCAGTTACATAAAGAAAAAG GAGTGCTACCCATGTTCTCATCCTTCAGAAGAATCCTGCGAACGGAGCTTCAGTAATATATCGTGGCCTTCACAT GTGAGGAAGCTACTTAACACTAGTTACTCTCACAATGAAGGACCTGGAATGAAAAATCTGTGTCTAAACAAGTCC TCTTTAGATTTTAGTGCAAATCCAGAGCCAGCGTCGGTTGCCTCGAGTAATTCTTTCATGGGTACCTTTGGAAAA GCTCTCAGGAGACCTCACCTAGATGCCTATTCAAGCTTTGGACAGCCATCAGATTGTCAGCCAAGAGCCTTTTAT GAAAATCACATTTGTACCTTTAAACAGACTTTAGAAAACTACAGGACTCCAAATTTTCAGTCTTATGACTTGGAC AAAAAGTTATGAAAATTTTTATACTGGGAATGATGCTCATATAAGAATACCTTTTTAAACTATTTTTAACTTTG TTTTATGCAAAAAGTATCTTACGTAAATTAATGATATAAATCATGATTATTTTATGTATTTTATAATGCCAGA TTTCTTTTTATGGAAAATGAGTTACTAAAGCATTTTAAATAATACCTGCCTTGTACCATTTTTTAAATAGAAGTT

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FIGURE 352

MSAPSLRARAGLGLLLCAVLGRAGRSDSGGRGELGQPSGVAAERPCPTTCRCLGDLLDCSRKRLARLPEPLPSW VARLDLSHNRLSFIKASSMSHLQSLREVKLNNNELETIPNLGPVSANITLLSLAGNRIVEILPEHLKEFQSLETL DLSSNNISELQTAFPALQLKYLYLNSNRVTSMEPGYFDNLANTLLVLKLNRNRISAIPPKMFKLPQLQHLELNRN KIKNVDGLTFQGLGALKSLKMQRNGVTKLMDGAFWGLSNMEILQLDHNNLTEITKGWLYGLLMLQELHLSQNAIN RISPDAWEFCQKLSELDLTFNHLSRLDDSSFLGLSLLNTLHIGNNRVSYIADCAFRGLSSLKTLDLKNNEISWTI EDMNGAFSGLDKLRRLILQGNRIRSITKKAFTGLDALEHLDLSDNAIMSLQGNAFSQMKKLQQLHLNTSSLLCDC QLKWLPQWVAENNFQSFVNASCAHPQLLKGRSIFAVSPDGFVCDDFPKPQITVQPETQSAIKGSNLSFICSAASS SDSPMTFAWKKDNELLHDAEMENYAHLRAQGGEVMEYTTILRLREVEFASEGKYQCVISNHFGSSYSVKAKLTVN MLPSFTKTPMDLTIRAGAMARLECAAVGHPAPQIAWQKDGGTDFPAARRRRMHVMPEDDVFFIVDVKIEDIGVYS CTAQNSAGSISANATLTVLETPSFLRPLLDRTVTKGETAVLQCIAGGSPPPKLNWTKDDSPLVVTERHFFAAGNQ LLIIVDSDVSDAGKYTCEMSNTLGTERGNVRLSVIPTPTCDSPQMTAPSLDDDGWATVGVVIIAVVCCVVGTSLV WVVIIYHTRRNEDCSITNTDETNLPADIPSYLSSQGTLADRQDGYVSSESGSHHQFVTSSGAGFFLPQHDSSGT CHIDNSSEADVEAATDLFLCPFLGSTGPMYLKGNVYGSDPFETYHTGCSPDPRTVLMDHYEPSYIKKKECYPCSH PSEESCERSFSNISWPSHVRKLLNTSYSHNEGPGMKNLCLNKSSLDFSANPEPASVASSNSFMGTFGKALRRPHL DAYSSFGQPSDCQPRAFYLKAHSSPDLDSGSEEDGKERTDFQEENHICTFKQTLENYRTPNFQSYDLDT

Important features:

Signal sequence:

amino acids 1-27

Transmembrane domain:

amino acids 808-828

N-glycosylation site.

amino acids 122-126, 156-160, 274-278, 442-446, 469-473, 515-519, 688-692, 729-733, 905-909, 987-991, 999-1003, 1016-1020

Glycosaminoglycan attachment site.

amino acids 886-890

Casein kinase II phosphorylation site.

amino acids 99-103, 180-184, 263-267, 314-318, 324-328, 374-378, 383-387, 407-411, 524-528, 608-612, 692-696, 709-713, 731-735, 799-803, 843-847, 863-867, 907-911, 1003-1007, 1018-1022, 1073-1077, 1079-1083, 1081-1085

Tyrosine kinase phosphorylation site.

amino acids 667-675

N-myristoylation site.

amino acids 14-20, 36-42, 239-245, 257-263, 380-386, 427-433, 513-519, 588-594, 672-678, 683-687, 774-780, 933-939

Leucine zipper pattern.

amino acids 58-80, 65-87

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FIGURE 353

AGCACTAAATGAACTTGAATTGTGTCTGTGGCGAGCAGGATGGTCGCTGTTACTTTGTGATGAGATCGGGGATGA ATTGCTCGCTTTAAAAATGCTGCTTTGGATTCTGTTGCTGGAGACGTCTCTTTGTTTTGCCGCTGGAAACGTTAC AGGGGACGTTTGCAAAGAGATCTGTTCCTGCAATGAGATAGAAGGGGACCTACACGTAGACTGTGAAAAAAA CACTCGACTTTTCCCTAATGAGTTCGCTAACTTTTATAATGCGGTTAGTTTGCACATGGAAAACAATGGCTTGCA TGAAATCGTTCCGGGGGCTTTTCTGGGGCTGCAGCTGGTGAAAAGGCTGCACATCAACAACAACAACAAGATCAAGTC TTTTCGAAAGCAGACTTTTCTGGGGCTGGACGATCTGGAATATCTCCAGGCTGATTTTAATTTATTACGAGATAT AGACCCGGGGGCCTTCCAGGACTTGAACAAGCTGGAGGTGCTCATTTTAAATGACAATCTCATCAGCACCCTACC TGCCAACGTGTTCCAGTATGTGCCCATCACCCACCTCGACCTCCGGGGTAACAGGCTGAAAACGCTGCCCTATGA GGAGGTCTTGGAGCAAATCCCTGGTATTGCGGAGATCCTGCTAGAGGATAACCCTTGGGACTGCACCTGTGATCT GCTCTCCCTGAAGAATGGCTGGAAAACATTCCCAAGAATGCCCTGATCGGCCGAGTGGTCTGCGAAGCCCCCAC TCTCCCGGCGCCCCTGCCCAAGAAGAGACCTTTGCTCCTGGACCCCTGCCAACTCCTTTCAAGACAAATGGGCA AGAGGATCATGCCACACCAGGGTCTGCTCCAAACGGAGGTACAAAGATCCCAGGCAACTGGCAGATCAAAATCAG ACCCACAGCAGCGATAGCGACGGGTAGCTCCAGGAACAAACCCTTAGCTAACAGTTTACCCTGCCCTGGGGGGCTG ${\tt CAGCTGCGACCACATCCCAGGGTCGGGTTTAAAGATGAACTGCAACAACAGGAACGTGAGCAGCTTGGCTGATTT}$ GAAGCCCAAGCTCTCTAACGTGCAGGAGCTTTTCCTACGAGATAACAAGATCCACAGCATCCGAAAATCGCACTT TGTGGATTACAAGAACCTCATTCTGTTGGATCTGGGCAACAATAACATCGCTACTGTAGAGAACAACACTTTCAA GAACCTTTTGGACCTCAGGTGGCTATACATGGATAGCAATTACCTGGACACGCTGTCCCGGGAGAAATTCGCGGG GCTGCAAAACCTAGAGTACCTGAACGTGGAGTACAACGCTATCCAGCTCATCCTCCCGGGCACTTTCAATGCCAT GCTCTCTAAACTCAGCCTGCACAACAATTACTTCATGTACCTCCCGGTGGCAGGGGTGCTGGACCAGTTAACCTC CATCATCCAGATAGACCTCCACGGAAACCCCTGGGAGTGCTCCTGCACAATTGTGCCTTTCAAGCAGTGGGCAGA ACGCTTGGGTTCCGAAGTGCTGATGAGCGACCTCAAGTGTGAGACGCCGGTGAACTTCTTTAGAAAGGATTTCAT GCTCCTCCCAATGACGAGATCTGCCCTCAGCTGTACGCTAGGATCTCGCCCACGTTAACTTCGCACAGTAAAAA GGTCCCGGGACTGCTGGTGTTTTGTCACCTCCGCCTTCACCGTGGTGGGCATGCTCGTGTTTATCCTGAGGAA TTCCTACTGGCACAATGGGCCTTACAACGCAGATGGGGCCCACAGAGTGTATGACTGTGGCTCTCACTCGCTCTC GCGCAGCCAGCTCGCTCTTTGCTGAGAGCCCCTTTTGACAGAAAGCCCAGCACGACCCTGCTGGAAGAACTGACA GTGCCCTCGCCCTCGGCCCCGGGGCCTGTGGGGTTGGATGCCGCGGTTCTATACATATATACATATATCCACATC TATATAGAGAGATAGATATCTATTTTTCCCCTGTGGATTAGCCCCGTGATGGCTCCCTGTTGGCTACGCAGGGAT GGGCAGTTGCACGAAGGCATGAATGTATTGTAAATAAGTAACTTTGACTTCTGAC

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FIGURE 354

MLLWILLLETSLCFAAGNVTGDVCKEKICSCNEIEGDLHVDCEKKGFTSLQRFTAPTSQFYHL
FLHGNSLTRLFPNEFANFYNAVSLHMENNGLHEIVPGAFLGLQLVKRLHINNNKIKSFRKQTF
LGLDDLEYLQADFNLLRDIDPGAFQDLNKLEVLILNDNLISTLPANVFQYVPITHLDLRGNRL
KTLPYEEVLEQIPGIAEILLEDNPWDCTCDLLSLKEWLENIPKNALIGRVVCEAPTRLQGKDL
NETTEQDLCPLKNRVDSSLPAPPAQEETFAPGPLPTPFKTNGQEDHATPGSAPNGGTKIPGNW
QIKIRPTAAIATGSSRNKPLANSLPCPGGCSCDHIPGSGLKMNCNNRNVSSLADLKPKLSNVQ
ELFLRDNKIHSIRKSHFVDYKNLILLDLGNNNIATVENNTFKNLLDLRWLYMDSNYLDTLSRE
KFAGLQNLEYLNVEYNAIQLILPGTFNAMPKLRILILNNNLLRSLPVDVFAGVSLSKLSLHNN
YFMYLPVAGVLDQLTSIIQIDLHGNPWECSCTIVPFKQWAERLGSEVLMSDLKCETPVNFFRK
DFMLLSNDEICPQLYARISPTLTSHSKNSTGLAETGTHSNSYLDTSRVSISVLVPGLLLVFVT
SAFTVVGMLVFILRNRKRSKRRDANSSASEINSLQTVCDSSYWHNGPYNADGAHRVYDCGSHS
LSD

Important features:

Signal sequence:

amino acids 1-15

Transmembrane domain:

amino acids 618-638

N-glycosylation site.

amino acids 18-22, 253-257, 363-367, 416-420, 595-599, 655-659

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 122-126, 646-650

Casein kinase II phosphorylation site.

amino acids 30-34, 180-184, 222-226, 256-260, 366-370, 573-577, 608-612, 657-661, 666-670, 693-697

N-myristoylation site.

amino acids 17-23, 67-73, 100-106, 302-308, 328-334, 343-349, 354-360, 465-471, 493-499, 598-604, 603-609

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 337-348

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FIGURE 355

AGTCGACTGCGTCCCCTGTACCCGGCGCCAGCTGTGTTCCTGACCCCAGAATAACTCAGGGCTGCACCGGGCCTG GCAGCGCTCCGCACACATTTCCTGTCGCGGCCTAAGGGAAACTGTTGGCCGCTGGGCCCGCGGGGGGATTCTTGG GGCGGTGACCGCGCTCCAGACACGCTCTGCGTCCTCGAGCGGGACAGATCCAAGTTGGGAGCAGCTCTGCGTGC CGAACACCCCACTGCCGACCGTGCTGGCTCGGCCTCGGGGGGCCTGCTACAGCCTGCACCACGCTACCATGAA $\tt CGCTGTGCTCCCGCGCTCCTGCGGGCCCAGGGCCCGGAGGGGGGCTCCAAAGACCTGCTGTTCTGGGTCGCACT$ GGAGCGCAGGCGTTCCCACTGCACCCTGGAGAACGAGCCTTTGCGGGGGTTTCTCCTGGCTGTCCTCCGACCCCGG CGGTCTCGAAAGCGACACGCTGCAGTGGGTGGAGGAGCCCCAACGCTCCTGCACCGCGCGGAGATGCGCGGTACT CCAGGCCACCGGTGGGGTCGAGCCCGCAGGCTGGAAGGAGATGCCACCTGCGCGCCCAACGGCTACCTGTG CAAGTACCAGTTTGAGGTCTTGTGTCCTGCGCCGCGCCCCGGGGCCGCCTCTAACTTGAGCTATCGCGCGCCCCTT CGAATGTGCTACGGGCTTCGAGCTGGGGAAGGACGGCCGCTCTTGTGTGACCAGTGGGGAAGGACAGCCGACCCT TGGGGGGACCGGGGTGCCCACCAGGCGCCGGCCACTGCAACCAGCCCCGTGCCGCAGAGAACATGGCCAAT CAGGGTCGACGAGAAGCTGGGAGAGACACCACTTGTCCCTGAACAAGACAATTCAGTAACATCTATTCCTGAGAT TCCTCGATGGGGATCACAGAGCACGATGTCTACCCTTCAAATGTCCCTTCAAGCCGAGTCAAAGGCCACTATCAC CCCATCAGGGAGCGTGATTTCCAAGTTTAATTCTACGACTTCCTCTGCCACTCCTCAGGCTTTCGACTCCTCCTC TGCCGTGGTCTTCATATTTGTGAGCACAGCAGTAGTAGTGTTGGTGATCTTGACCATGACAGTACTGGGGCTTGT GCGGGACAGAGCAGAGGGTGCCTTGCTGGCGGAGTCCCCTCTTGGCTCTAGTGATGCA<u>TAG</u>GGAAACAGGGGACA TTTCTGCAGAAATCCCCCTTCCTCTAAATTCCCTTTACTCCACTGAGGAGCTAAATCAGAACTGCACACCTCCTTC CCTGATGATAGAGGAAGTGCATTTAGGATGGTGATACTGGGGGACCGGGTAGTGCTGGGGAGAGATATT TTCTTATGTTTATTCGGAGAATTTGGAGAAGTGATTGAACTTTTCAAGACATTGGAAACAAATAGAACACAATAT AATTTACATTAAAAAATAATTTCTACCAAAATGGAAAGGAAATGTTCTATGTTGTTCAGGCTAGGAGTATATTGG TTCGAAATCCCAGGGAAAAAAATAAAAATAAAAATTAAAGGATTGTTGAT

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FIGURE 356

MRPAFALCLLWOALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGALST VRAGAELRAVLALLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSWLSSDPGGLESD TLQWVEEPQRSCTARRCAVLQATGGVEPAGWKEMRCHLRANGYLCKYQFEVLCPAPRPGAASN LSYRAPFQLHSAALDFSPPGTEVSALCRGQLPISVTCIADEIGARWDKLSGDVLCPCPGRYLR AGKCAELPNCLDDLGGFACECATGFELGKDGRSCVTSGEGOPTLGGTGVPTRRPPATATSPVP QRTWPIRVDEKLGETPLVPEQDNSVTSIPEIPRWGSQSTMSTLQMSLQAESKATITPSGSVIS KFNSTTSSATPQAFDSSSAVVFIFVSTAVVVLVILTMTVLGLVKLCFHESPSSQPRKESMGPP GLESDPEPAALGSSSAHCTNNGVKVGDCDLRDRAEGALLAESPLGSSDA

Important features:

Signal sequence:

amino acids 1-16.

Transmembrane domain:

amino acids 399-418

N-glycosylation site.

amino acids 189-193, 381-385

Glycosaminoglycan attachment site.

amino acids 289-293

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 98-102, 434-438

Casein kinase II phosphorylation site.

amino acids 275-279, 288-292, 342-346, 445-449

N-myristoylation site.

amino acids 30-36, 35-41, 58-64, 59-65, 121-127, 151-157, 185-191, 209-215, 267-273, 350-356, 374-380, 453-459, 463-469, 477-483

Aspartic acid and asparagine hydroxylation site.

amino acids 262-274

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FIGURE 357

CCCATCTCAAGCTGATCTTGGCACCTCTCATGCTCTGCTCTTCAACCAGACCTCTACATTCCATTTTGGAAGA AGACTAAAAA**TG**GTGTTTCCAATGTGGACACTGAAGAGACAAATTCTTATCCTTTTTAACATAATCCTAATTTCC AAACTCCTTGGGGCTAGATGGTTTCCTAAAACTCTGCCCTGTGATGTCACTCTGGATGTTCCAAAGAACCATGTG ATCGTGGACTGCACAGACAAGCATTTGACAGAAATTCCTGGAGGTATTCCCACGAACACCACGAACCTCACCCTC ACCATTAACCACATACCAGACATCTCCCCAGCGTCCTTTCACAGACTGGACCATCTGGTAGAGATCGATTTCAGA TGCAACTGTGTACCTATTCCACTGGGGTCAAAAAAACAACATGTGCATCAAGAGGCTGCAGATTAAACCCAGAAGC CCTAGCTTACAGCTTCTCAGCCTTGAGGCCAACAACATCTTTTCCATCAGAAAAGAGAATCTAACAGAACTGGCC AACATAGAAATACTCTACCTGGGCCAAAACTGTTATTATCGAAATCCTTGTTATGTTTCATATTCAATAGAGAAA GATGCCTTCCTAAACTTGACAAAGTTAAAAGTGCTCTCCCTGAAAGATAACAATGTCACAGCCGTCCCTACTGTT TTGCCATCTACTTTAACAGAACTATATCTCTACAACAACATGATTGCAAAAATCCAAGAAGATGATTTTAATAAC CTCAACCAATTACAAATTCTTGACCTAAGTGGAAATTGCCCTCGTTGTTATAATGCCCCATTTCCTTGTGCGCCG TGTAAAAATAATTCTCCCCTACAGATCCCTGTAAATGCTTTTGATGCGCTGACAGAATTAAAAGTTTTACGTCTA CACAGTAACTCTCTTCAGCATGTGCCCCCAAGATGGTTTAAGAACATCAACAAACTCCAGGAACTGGATCTGTCC CAAAACTTCTTGGCCAAAGAAATTGGGGATGCTAAATTTCTGCATTTTCTCCCCAGCCTCATCCAATTGGATCTG TCTTTCAATTTTGAACTTCAGGTCTATCGTGCATCTATGAATCTATCACAAGCATTTTCTTCACTGAAAAGCCTG AAAATTCTGCGGATCAGAGGATATGTCTTTAAAGAGTTGAAAAGCTTTAACCTCTCGCCATTACATAATCTTCAA AATCTTGAAGTTCTTGGCACTAACTTTATAAAAATTGCTAACCTCAGCATGTTTAAACAATTTAAAAGA CTGAAAGTCATAGATCTTTCAGTGAATAAAATATCACCTTCAGGAGATTCAAGTGAAGTTGGCTTCTGCTCAAAT GCCAGAACTTCTGTAGAAAGTTATGAACCCCAGGTCCTGGAACAATTACATTATTTCAGATATGATAAGTATGCA AGGAGTTGCAGATTCAAAAACAAGGGCTTCTTTCATGTCTGTTAATGAAAGCTGCTACAAGTATGGGCAGACC AATCTGTCAGGAAATCTCATTAGCCAAACTCTTAATGGCAGTGAATTCCAACCTTTAGCAGAGCTGAGATATTTG GACTTCTCCAACAACCGGCTTGATTTACTCCATTCAACAGCATTTGAAGAGCTTCACAAACTGGAAGTTCTGGAT ATAAGCAGTAATAGCCATTATTTTCAATCAGAAGGAATTACTCATATGCTAAACTTTACCAAGAACCTAAAGGTT ACTCTGGAATTCAGAGGAAATCACTTAGATGTTTTATGGAGAGAGGTGATAACAGATACTTACAATTATTCAAG AATCTGCTAAAATTAGAGGAATTAGACATCTCTAAAAATTCCCTAAGTTTCTTGCCTTCTGGAGTTTTTGATGGT ATGCCTCCAAATCTAAAGAATCTCTCTTTGGCCAAAAATGGGCTCAAATCTTTCAGTTGGAAGAAACTCCAGTGT AGAAGCCTCAAGAATCTGATTCTTAAGAATAATCAAATCAGGAGTCTGACGAAGTATTTTCTACAAGATGCCTTC CAGTTGCGATATCTGGATCTCAGCTCAAATAAAATCCAGATGATCCAAAAGACCAGCTTCCCAGAAAATGTCCTC GTTAACCATACGGAGGTGACTATTCCTTACCTGGCCACAGATGTGACTTGTGTGGGGCCAGGAGCACAAGGGC ${\tt CAAAGTGTGATCTCCCTGGATCTGTACACCTGTGAGTTAGATCTGACTAACCTGATTCTGTTCTCACTTTCCATA}$ TCTGTATCTCTCTTTCTCATGGTGATGACAGCAAGTCACCTCTATTTCTGGGATGTGTGTATATTTACCAT TTCTGTAAGGCCAAGATAAAGGGGTATCAGCGTCTAATATCACCAGACTGTTGCTATGATGCTTTTATTGTGTAT GACACTAAAGACCCAGCTGTGACCGAGTGGGTTTTGGCTGAGCTGGTGGCCAAACTGGAAGACCCAAGAGAGAAA CATTTTAATTTATGTCTCGAGGAAAGGGACTGGTTACCAGGGCAGCCAGTTCTGGAAAACCTTTCCCAGAGCATA CAGCTTAGCAAAAAGACAGTGTTTGTGATGACAGACAAGTATGCAAAGACTGAAAATTTTAAGATAGCATTTTAC TTGTCCCATCAGAGGCTCATGGATGAAAAAGTTGATGTGATTATCTTGATATTTCTTGAGAAGCCCTTTCAGAAG TCCAAGTTCCTCCAGCTCCGGAAAAGGCTCTGTGGGAGTTCTGTCCTTGAGTGGCCAACAAACCCGCAAGCTCAC CCATACTTCTGGCAGTGTCTAAAGAACGCCCTGGCCACAGACAATCATGTGGCCTATAGTCAGGTGTTCAAGGAA ACGGTCTAGCCCTTCTTTGCAAAACACAACTGCCTAGTTTACCAAGGAGAGGCCTGGC

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FIGURE 358

MVFPMWTLKRQILILFNIILISKLLGARWFPKTLPCDVTLDVPKNHVIVDCTDKHLTEIPGGI PTNTTNLTLTINHIPDISPASFHRLDHLVEIDFRCNCVPIPLGSKNNMCIKRLQIKPRSFSGL TYLKSLYLDGNOLLEIPOGLPPSLQLLSLEANNIFSIRKENLTELANIEILYLGONCYYRNPC YVSYSIEKDAFLNLTKLKVLSLKDNNVTAVPTVLPSTLTELYLYNNMIAKIQEDDFNNLNQLQ ILDLSGNCPRCYNAPFPCAPCKNNSPLQIPVNAFDALTELKVLRLHSNSLQHVPPRWFKNINK LQELDLSQNFLAKEIGDAKFLHFLPSLIQLDLSFNFELQVYRASMNLSQAFSSLKSLKILRIR GYVFKELKSFNLSPLHNLONLEVLDLGTNFIKIANLSMFKOFKRLKVIDLSVNKISPSGDSSE VGFCSNARTSVESYEPOVLEOLHYFRYDKYARSCRFKNKEASFMSVNESCYKYGOTLDLSKNS IFFVKSSDFQHLSFLKCLNLSGNLISQTLNGSEFQPLAELRYLDFSNNRLDLLHSTAFEELHK LEVLDISSNSHYFQSEGITHMLNFTKNLKVLQKLMMNDNDISSSTSRTMESESLRTLEFRGNH LDVLWREGDNRYLQLFKNLLKLEELDISKNSLSFLPSGVFDGMPPNLKNLSLAKNGLKSFSWK KLQCLKNLETLDLSHNQLTTVPERLSNCSRSLKNLILKNNQIRSLTKYFLQDAFQLRYLDLSS NKIQMIQKTSFPENVLNNLKMLLLHHNRFLCTCDAVWFVWWVNHTEVTIPYLATDVTCVGPGA HKGQSVISLDLYTCELDLTNLILFSLSISVSLFLMVMMTASHLYFWDVWYIYHFCKAKIKGYQ RLISPDCCYDAFIVYDTKDPAVTEWVLAELVAKLEDPREKHFNLCLEERDWLPGQPVLENLSQ SIQLSKKTVFVMTDKYAKTENFKIAFYLSHQRLMDEKVDVIILIFLEKPFQKSKFLQLRKRLC GSSVLEWPTNPQAHPYFWQCLKNALATDNHVAYSQVFKETV

Important features:

Signal sequence:

amino acids 1-26

Transmembrane domain:

amino acids 840-860

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FIGURE 359

GACGGCTGGCCACCATGCACGGCTCCTGCAGTTTCCTGATGCTTCTGCTGCCGCTACTGCTAC TGCTGGTGGCCACCACGGCCCCGTTGGAGCCCTCACAGATGAGGAGAAACGTTTGATGGTGG AGCTGCACAACCTCTACCGGGCCCAGGTATCCCCGACGGCCTCAGACATGCTGCACATGAGAT GGGACGAGGAGCTGGCCGCCTTCGCCAAGGCCTACGCACGGCAGTGCGTGTGGGGCCACAACA AGGAGCGCGGCGCGCGCGAGAATCTGTTCGCCATCACAGACGAGGCCATGGACGTGCCGC TGGCCATGGAGGAGTGGCACCACGAGCGTGAGCACTACAACCTCAGCGCCGCCACCTGCAGCC CAGGCCAGATGTGCGGCCACTACACGCAGGTGGTATGGGCCAAGACAGAGAGGGTCGGCTGTG GTTCCCACTTCTGTGAGAAGCTCCAGGGTGTTGAGGAGACCAACATCGAATTACTGGTGTGCA ACTATGAGCCTCCGGGGAACGTGAAGGGGAAACGGCCCTACCAGGAGGGGACTCCGTGCTCCC AATGTCCCTCTGGCTACCACTGCAAGAACTCCCTCTGTGAACCCATCGGAAGCCCGGAAGATG CTCAGGATTTGCCTTACCTGGTAACTGAGGCCCCATCCTTCCGGGCGACTGAAGCATCAGACT CTAGGAAAATGGGTACTCCTTCCTTCCCTAGCAACGGGGATTCCGGCTTTCTTGGTAACAGAGG TCTCAGGCTCCCTGGCAACCAAGGCTCTGCCTGCTGTGGAAACCCAGGCCCCAACTTCCTTAG CAACGAAAGACCCGCCCTCCATGGCAACAGAGGCTCCACCTTGCGTAACAACTGAGGTCCCTT CCATTTTGGCAGCTCACAGCCTGCCTCCTTGGATGAGGAGCCAGTTACCTTCCCCAAATCGA GCCCAGAGAACTCTCTGGACCCCAAGATGTCCCTGACAGGGGCAAGGGAACTCCTACCCCATG CCCAGGAGGAGGCTGAGGCTGAGTTGCCTCCTTCCAGTGAGGTCTTGGCCTCAGTTT TTCCAGCCCAGGACAAGCCAGGTGAGCTGCAGGCCACACTGGACCACACGGGGCACACCTCCT CCAAGTCCCTGCCCAATTTCCCCAATACCTCTGCCACCGCTAATGCCACGGGTGGGCGTGCCC TGGCTCTGCAGTCGTCCTTGCCAGGTGCAGAGGGCCCTGACAAGCCTAGCGTTGTGTCAGGGC TGAACTCGGGCCCTGGTCATGTGTGGGGCCCTCTCCTGGGACTACTGCTCCTGCCTCCTCTGG TGTTGGCTGGAATCTTC**TGA**ATGGGATACCACTCAAAGGGTGAAGAGGTCAGCTGTCCTCCTG TCATCTTCCCCACCCTGTCCCCAGCCCCTAAACAAGATACTTCTTGGTTAAGGCCCTCCGGAA GCTGCGAGCTCAGGAGGCCGCCTGAGGACTGCACACCGGGCCCACACCTCTCCTGCCCCTCCC TCCTGAGTCCTGGGGGTGGGAGGATTTGAGGGAGCTCACTGCCTACCTGGCCTGGGGCTGTCT GCCCACACAGCATGTGCGCTCTCCCTGAGTGCCTGTGTAGCTGGGGATGGGGATTCCTAGGGG CAGATGAAGGACAAGCCCCACTGGAGTGGGGTTCTTTGAGTGGGGGAGGCAGGGACGAGGGAA GGAAAGTAACTCCTGACTCTCCAATAAAAACCTGTCCAACCTGTGAAA

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FIGURE 360

MHGSCSFLMLLLPLLLLVATTGPVGALTDEEKRLMVELHNLYRAQVSPTASDMLHMRWDEEL
AAFAKAYARQCVWGHNKERGRRGENLFAITDEGMDVPLAMEEWHHEREHYNLSAATCSPGQMC
GHYTQVVWAKTERIGCGSHFCEKLQGVEETNIELLVCNYEPPGNVKGKRPYQEGTPCSQCPSG
YHCKNSLCEPIGSPEDAQDLPYLVTEAPSFRATEASDSRKMGTPSSLATGIPAFLVTEVSGSL
ATKALPAVETQAPTSLATKDPPSMATEAPPCVTTEVPSILAAHSLPSLDEEPVTFPKSTHVPI
PKSADKVTDKTKVPSRSPENSLDPKMSLTGARELLPHAQEEAEAEAELPPSSEVLASVFPAQD
KPGELQATLDHTGHTSSKSLPNFPNTSATANATGGRALALQSSLPGAEGPDKPSVVSGLNSGP
GHVWGPLLGLLLLPPLVLAGIF

Important features:

Signal sequence:

amino acids 1-22

N-glycosylation site.

amino acids 114-118, 403-407, 409-413

Glycosaminoglycan attachment site.

amino acids 439-443

Casein kinase II phosphorylation site.

amino acids 29-33, 50-54, 156-160, 195-199, 202-206, 299-303

N-myristoylation site.

amino acids 123-129, 143-149, 152-158, 169-175, 180-186, 231-237, 250-256

Amidation site.

amino acids 82-86, 172-176

Peroxidases proximal heme-ligand signature.

amino acids 287-298

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 signature 1.

amino acids 127-138

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 signature 2.

amino acids 160-172

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FIGURE 361

GACTAGTTCTCTTGGAGTCTGGGAGGAGGAAAGCGGAGCCGGCAGGGAGCGAACCAGGACTGG GGTGACGGCAGGGCAGGGGGCGCCTGGCCGGGGGAGAAGCGCGGGGGCTGGAGCACCAACT GGAGGGTCCGGAGTAGCGAGCGCCCCGAAGGAGGCCATCGGGGAGCCGGGAGGGGGGACTGCG AGAGGACCCCGGCGTCCGGGCTCCCGGTGCCAGCGCTATCAGGCCCACTCCTCGTCCTGCTGCT CCTGGGCCTGGCGGCCCGCCCCCACTGGACGACAACAAGATCCCCAGCCTCTGCCCGGG GCACCCGGCCTTCCAGGCACGCCGGGCCACCATGGCAGCCAGGGCTTGCCGGGCCGCGATGG CCGCGACGCCGCGACGCGCGCCCCGGGGCTCCGGGAGAAAAGGCGAGGCGGGAGGCCGGG ACTGCCGGGACCTCGAGGGGACCCCGGGCCGCGAGGAGAGGCGGGACCCGCGGGGCCCACCGG GCCTGCCGGGGAGTGCTCGGTGCCTCCGCGATCCGCCTTCAGCGCCAAGCGCTCCGAGAGCCG GGTGCCTCCGCCGTCTGACGCACCCTTGCCCTTCGACCGCGTGCTGGTGAACGAGCAGGGACA TTACGACGCCGTCACCGGCAAGTTCACCTGCCAGGTGCCTGGGGTCTACTACTTCGCCGTCCA TGCCACCGTCTACCGGGCCAGCCTGCAGTTTGATCTGGTGAAGAATGGCGAATCCATTGCCTC GCTGGAGCCTGAGGACCAAGTGTGGGTGCAGGTGGGTGTGGCTGACTACATTGGCATCTATGC CAGCATCAAGACAGCACCTTCTCCGGATTTCTGGTGTACTCCGACTGGCACAGCTCCCC AGTCTTTGCTTAGTGCCCACTGCAAAGTGAGCTCATGCTCTCACTCCTAGAAGGAGGGTGTGA GGCTGACAACĆAGGTCATCCAGGAGGGCTGGCCCCCCTGGAATATTGTGAATGACTAGGGAGG TGGGGTAGAGCACTCTCCGTCCTGCTGCTGGCAAGGAATGGGAACAGTGGCTGTCTGCGATCA CAAGTGTAAGTCCCCCAGTTGCTCTGGTCCAGGAGCCCACGGTGGGGTGCTCTCTTCCTGGTC

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FIGURE 362

MRPLLVLLLLGLAAGSPPLDDNKIPSLCPGHPGLPGTPGHHGSQGLPGRDGRDGAPGAPG EKGEGGRPGLPGPRGDPGPRGEAGPAGPTGPAGECSVPPRSAFSAKRSESRVPPPSDAPLPFD RVLVNEQGHYDAVTGKFTCQVPGVYYFAVHATVYRASLQFDLVKNGESIASFFQFFGGWPKPA SLSGGAMVRLEPEDQVWVQVGVGDYIGIYASIKTDSTFSGFLVYSDWHSSPVFA

Important features:

Signal sequence.

amino acids 1-15

N-myristoylation sites.

amino acids 11-17, 68-74, 216-222

Cell attachment sequence.

amino acids 77-80

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FIGURE 363

GGAGAGCGGAGCGAAGCTGGATAACAGGGGACCGATGATGTGGCGACCATCAGTTCTGCTGCT TCTGTTGCTACTGAGGCACGGGGCCCAGGGGAAGCCATCCCCAGACGCAGGCCCTCATGGCCA GGGGAGGTGCACCAGGCGCCCCCTGAGCGACGCTCCCCATGATGACGCCCACGGGAACTT CCAGTACGACCATGAGGCTTTCCTGGGACGGGAAGTGGCCAAGGAATTCGACCAACTCACCCC AGAGGAAAGCCAGGCCCGTCTGGGGCGGATCGTGGACCGCATGGACCGCGCGGGGGACGGCGA CGGCTGGGTGTCGCCGAGCTTCGCGCGTGGATCGCGCACACGCAGCAGCGGCACATACG GGACTCGGTGAGCGCGGCCTGGGACACGTACGACACGGACCGCGACGGCGTGTGGGTTGGGA GGAGCTGCGCAACGCCACCTATGGCCACTACGCGCCCGGTGAAGAATTTCATGACGTGGAGGA TGCAGAGACCTACAAAAAGATGCTGGCTCGGGACGAGCGGCGTTTCCGGGTGGCCGACCAGGA TGGGGACTCGATGGCCACTCGAGAGGAGCTGACAGCCTTCCTGCACCCCGAGGAGTTCCCTCA CATGCGGGACATCGTGATTGCTGAAACCCTGGAGGACCTGGACAGAAACAAAGATGGCTATGT CCAGGTGGAGGAGTACATCGCGGATCTGTACTCAGCCGAGCCTGGGGAGGAGGAGCCGGCGTG GGTGCAGACGGAGAGCCAGTTCCGGGACTTCCGGGATCTGAACAAGGATGGGCACCTGGA TGGGAGTGAGGTGGCCACTGGGTGCTGCCCCTGCCCAGGACCAGCCCCTGGTGGAAGCCAA CCACCTGCTGCACGAGAGCGACACGGACAAGGATGGGCGGCTGAGCAAAGCGGAAATCCTGGG TAATTGGAACATGTTTGTGGGCAGTCAGGCCACCAACTATGGCGAGGACCTGACCCGGCACCA CGATGAGCTGTGAGCACCGCGCACCTGCCACAGCCTCAGAGGCCCGCACAATGACCGGAGGAG GGGCCGCTGTGGCCCCCTCCCTGTCCAGGCCCCGCAGGAGGCAGATGCAGTCCCAGGC ATCCTCCTGCCCCTGGGCTCTCAGGGACCCCCTGGGTCGGCTTCTGTCCCTGTCACACCCCCA GCCTGGCCTGGGACACCTCCTCTCTGCCAGGAGGCAATAAAAGCCAGCGCCGGGACCTTGAAA

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FIGURE 364

MMWRPSVLLLLLLRHGAQGKPSPDAGPHGQGRVHQAAPLSDAPHDDAHGNFQYDHEAFLGRE VAKEFDQLTPEESQARLGRIVDRMDRAGDGDGWVSLAELRAWIAHTQQRHIRDSVSAAWDTYD TDRDGRVGWEELRNATYGHYAPGEEFHDVEDAETYKKMLARDERRFRVADQDGDSMATREELT AFLHPEEFPHMRDIVIAETLEDLDRNKDGYVQVEEYIADLYSAEPGEEEPAWVQTERQQFRDF RDLNKDGHLDGSEVGHWVLPPAQDQPLVEANHLLHESDTDKDGRLSKAEILGNWNMFVGSQAT NYGEDLTRHHDEL

Important features:

Signal sequence:

amino acids 1-20

N-glycosylation site.

amino acids 140-144

Casein kinase II phosphorylation site.

amino acids 72-76, 98-102, 127-131, 184-188, 208-212, 289-293, 291-295, 298-302

N-myristoylation site.

amino acids 263-269, 311-317

Endoplasmic reticulum targeting sequence.

amino acids 325-330

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FIGURE 365

GTCTGTTCCCAGGAGTCCTTCGGCGGCTGTTGTGTCAGTGGCCTGATCGCG**ATG**GGGACAAAG GCGCAAGTCGAGAGGAAACTGTTGTGCCTCTTCATATTGGCGATCCTGTTGTGCTCCCTGGCA TTGGGCAGTGTTACAGTGCACTCTTCTGAACCTGAAGTCAGAATTCCTGAGAATAATCCTGTG AAGTTGTCCTGTGCCTACTCGGGCTTTTCTTCTCCCCGTGTGGAGTGGAAGTTTGACCAAGGA GACACCACCAGACTCGTTTGCTATAATAACAAGATCACAGCTTCCTATGAGGACCGGGTGACC TTCTTGCCAACTGGTATCACCTTCAAGTCCGTGACACGGGAAGACACTGGGACATACACTTGT ATGGTCTCTGAGGAAGGCGGCAACAGCTATGGGGAGGTCAAGGTCAAGCTCATCGTGCTTGTG CCTCCATCCAAGCCTACAGTTAACATCCCCTCCTCTGCCACCATTGGGAACCGGGCAGTGCTG ACATGCTCAGAACAAGATGGTTCCCCACCTTCTGAATACACCTGGTTCAAAGATGGGATAGTG ATGCCTACGAATCCCAAAAGCACCCGTGCCTTCAGCAACTCTTCCTATGTCCTGAATCCCACA ACAGGAGAGCTGGTCTTTGATCCCCTGTCAGCCTCTGATACTGGAGAATACAGCTGTGAGGCA CGGAATGGGTATGGGACACCCATGACTTCAAATGCTGTGCGCATGGAAGCTGTGGAGCGGAAT GTGGGGGTCATCGTGGCAGCCGTCCTTGTAACCCTGATTCTCCTGGGAATCTTGGTTTTTTGGC GTGATTTACAGCCAGCCTAGTGCCCGAAGTGAAGGAGAATTCAAACAGACCTCGTCATTCCTG $\mathtt{GTG}^{\mathtt{TGA}}_{\mathtt{GCCTGGTCGGCTCACCGCCTATCATCTGCATTTGCCTTACTCAGGTGCTACCGGACT}$ CTGGCCCTGATGTCTGTAGTTTCACAGGATGCCTTATTTGTCTTCTACACCCCACAGGGCCC CCTACTTCTTCGGATGTTTTTTTAATAATGTCAGCTATGTGCCCCATCCTTCATGCCCTC CCTCCCTTTCCTACCACTGCTGAGTGGCCTGGAACTTGTTTAAAGTGTTTATTCCCCATTTCT TTGAGGGATCAGGAAGGAATCCTGGGTATGCCATTGACTTCCCTTCTAAGTAGACAGCAAAAA TATCTTGAGCTTGGTTCTGGGCTCTTTCCTTGTGTACTGACGACCAGGGCCAGCTGTTCTAGA GCGGGAATTAGAGGCTAGAGCGGCTGAAATGGTTGTTTGGTGATGACACTGGGGTCCTTCCAT CTCTGGGGCCCACTCTCTTCTGTCTTCCCATGGGAAGTGCCACTGGGATCCCTCTGCCCTGTC CTCCTGAATACAAGCTGACTGACATTGACTGTGTCTGTGGAAAATGGGAGCTCTTGTTGTGGA GAGCATAGTAAATTTTCAGAGAACTTGAAGCCAAAAGGATTTAAAACCGCTGCTCTAAAGAAA CACCTGAGGTCGGGAGTTCGGGATCAGCCTGACCAACATGGAGAAACCCTACTGGAAATACAA AGTTAGCCAGGCATGGTGGTGCATGCCTGTAGTCCCAGCTGCTCAGGAGCCTGGCAACAAGAG CAAAACTCCAGCTCAAAAAAAAAAAAAAAAA

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FIGURE 366

MGTKAQVERKLLCLFILAILLCSLALGSVTVHSSEPEVRIPENNPVKLSCAYSGFSSPRVEWK
FDQGDTTRLVCYNNKITASYEDRVTFLPTGITFKSVTREDTGTYTCMVSEEGGNSYGEVKVKL
IVLVPPSKPTVNIPSSATIGNRAVLTCSEQDGSPPSEYTWFKDGIVMPTNPKSTRAFSNSSYV
LNPTTGELVFDPLSASDTGEYSCEARNGYGTPMTSNAVRMEAVERNVGVIVAAVLVTLILLGI
LVFGIWFAYSRGHFDRTKKGTSSKKVIYSOPSARSEGEFKOTSSFLV

Important features:

Signal sequence:

amino acids 1-27

Transmembrane domain:

amino acids 238-255

N-glycosylation site.

amino acids 185-189

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 270-274

Casein kinase II phosphorylation site.

amino acids 34-38, 82-86, 100-104, 118-122, 152-156, 154-158, 193-197, 203-207, 287-291

N-myristoylation site.

amino acids 105-111, 116-122, 158-164, 219-225, 237-243, 256-262

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FIGURE 367

GAAGCTTTTTCTTGTGAGCCCTGGATCTTAACACAAATGTGTATATGTGCACACAGGGAGCATTCAAGAATGAAA CCACCCCAAAAAAAAGGATGATTGGAAATGAAGAACCGAGGATTCACAAAGAAAAAAGTATGTTCATTTTTCTC TATAAAGGAGAAAGTGAGCCAAGGAGATATTTTTGGAATGAAAAGTTTGGGGCTTTTTTAGTAAAGTAAAGAACT GGTGTGGTGGTGTTTTCCTTTTTTGAATTTCCCACAGAGGGAGAGAATTAATAATACATCTGCAAAGAAA TTTTATTCCTTTTGGTATCAAGATCATGCGTTTTCTCTTGTTCTTAACCACCTGGATTTCCATCTGGATGTTGCT $\tt GTGATCAGTCTGAAATACAACTGTTTGAATTCCAGAAGGACCAACACCAGATAAATTATGA{\color{red}{\textbf{ATG}}}{\textbf{TTGAACAAGAT}}$ GACCTTACATCCACAGCAGATAATGATAGGTCCTAGGTTTAACAGGGCCCTATTTTGACCCCCTGCTTGTGGTGCT GCTGGCTCTTCAACTTCTTGTGGTGGCTGGTCTGGTGCGGGCTCAGACCTGCCCTTCTGTGTGCTCCTGCAGCAA GCTGAACCTCCATGAGAACCAAATCCAGATCATCAAAGTGAACAGCTTCAAGCACTTGAGGCACTTGGAAATCCT ACAGTTGAGTAGGAACCATATCAGAACCATTGAAATTGGGGCTTTCAATGGTCTGGCGAACCTCAACACTCTGGA ACTCTTTGACAATCGTCTTACTACCATCCCGAATGGAGCTTTTGTATACTTGTCTAAACTGAAGGAGCTCTGGTT GCGAAACAACCCCATTGAAAGCATCCCTTCTTATGCTTTTAACAGAATTCCTTCTTTGCGCCGACTAGACTTAGG GGAATTGAAAAGACTTTCATACATCTCAGAAGGTGCCTTTGAAGGTCTGTCCAACTTGAGGTATTTGAACCTTGC CATGTGCAACCTTCGGGAAATCCCTAACCTCACACCGCTCATAAAACTAGATGAGCTGGATCTTTCTGGGAATCA TTTATCTGCCATCAGGCCTGGCTCTTTCCAGGGTTTGATGCACCTTCAAAAACTGTGGATGATACAGTCCCAGAT TCAAGTGATTGAACGGAATGCCTTTGACAACCTTCAGTCACTAGTGGAGATCAACCTGGCACACAATAATCTAAC ATTACTGCCTCATGACCTCTTCACTCCCTTGCATCATCTAGAGCGGATACATTTACATCACAACCCTTGGAACTG TAACTGTGACATACTGTGGCTCAGCTGGTGGATAAAAGACATGGCCCCCTCGAACACAGCTTGTTGTGCCCGGTG TAACACTCCTCCCAATCTAAAGGGGAGGTACATTGGAGAGCTCGACCAGAATTACTTCACATGCTATGCTCCGGT GATTGTGGAGCCCCCTGCAGACCTCAATGTCACTGAAGGCATGGCAGCTGAAATGTCGGGCCTCCACATC CCTGACATCTGTATCTTGGATTACTCCAAATGGAACAGTCATGACACATGGGGCGTACAAAGTGCGGATAGCTGT GCTCAGTGATGGTACGTTAAATTTCACAAATGTAACTGTGCAAGATACAGGCATGTACACATGTATGGTGAGTAA TTCCGTTGGGAATACTACTGCTTCAGCCACCCTGAATGTTACTGCAGCAACCACTACTCCTTTCTCTTACTTTTC AACCGTCACAGTAGAGACTATGGAACCGTCTCAGGATGAGGCACGGACCACAGATAACAATGTGGGTCCCACTCC AGTGGTCGACTGGGAGACCACCAATGTGACCACCTCTCTCACACCACAGAGCACAAGGTCGACAGAGAAAAACCTT CACCATCCCAGTGACTGATATAAACAGTGGGATCCCAGGAATTGATGAGGTCATGAAGACTACCAAAATCATCAT TGGGTGTTTTGTGGCCATCACACTCATGGCTGCAGTGATGCTGGTCATTTTCTACAAGATGAGGAAGCAGCACCA TCGGCAAAACCATCACGCCCCAACAAGGACTGTTGAAATTATTAATGTGGATGATGAGATTACGGGAGACACACC CATGGAAAGCCACCTGCCCATGCCTATCGAGCATGAGCACCTAAATCACTATAACTCATACAAATCTCCCTT CAACCACACAACAACAGTTAACACAATAAATTCAATACACAGTTCAGTGCATGAACCGTTATTGATCCGAATGAA AAAAGAAAAGAAATTTATTTATTAAAAATTCTATTGTGATCTAAAGCAGACAAAAA

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FIGURE 368

MLNKMTLHPQQIMIGPRFNRALFDPLLVVLLALQLLVVAGLVRAQTCPSVCSCSNQFSKVICVRKNLREVPDGIS
TNTRLLNLHENQIQIIKVNSFKHLRHLEILQLSRNHIRTIEIGAFNGLANLNTLELFDNRLTTIPNGAFVYLSKL
KELWLRNNPIESIPSYAFNRIPSLRRLDLGELKRLSYISEGAFEGLSNLRYLNLAMCNLREIPNLTPLIKLDELD
LSGNHLSAIRPGSFQGLMHLQKLWMIQSQIQVIERNAFDNLQSLVEINLAHNNLTLLPHDLFTPLHHLERIHLHH
NPWNCNCDILWLSWWIKDMAPSNTACCARCNTPPNLKGRYIGELDQNYFTCYAPVIVEPPADLNVTEGMAAELKC
RASTSLTSVSWITPNGTVMTHGAYKVRIAVLSDGTLNFTNVTVQDTGMYTCMVSNSVGNTTASATLNVTAATTTP
FSYFSTVTVETMEPSQDEARTTDNNVGPTPVVDWETTNVTTSLTPQSTRSTEKTFTIPVTDINSGIPGIDEVMKT
TKIIIGCFVAITLMAAVMLVIFYKMRKQHHRQNHHAPTRTVEIINVDDEITGDTPMESHLPMPAIEHEHLNHYNS
YKSPFNHTTTVNTINSIHSSVHEPLLIRMNSKDNVQETQI

Important features:

Signal sequence:

amino acids 1-44

Transmembrane domain:

amino acids 523-543

N-glycosylation site.

amino acids 278-282, 364-368, 390-394, 412-416, 415-419, 434-438, 442-446, 488-492, 606-610

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 183-187

Casein kinase II phosphorylation site.

amino acids 268-272, 417-421, 465-469, 579-583, 620-624

N-myristoylation site.

amino acids 40-46, 73-79, 118-124, 191-197, 228-234, 237-243, 391-397, 422-428, 433-439, 531-537

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FIGURE 369

CAAAACTTGCGTCGCGGAGAGCGCCCAGCTTGACTTGAATGGAAGGAGCCCGAGCCCGCGGAGCGCAGCTGAGAC CTGCTCCACGAGGCGCCACTGGTGTAACCGGGAGAGCCCCTGGGTGGTCCCGTCCCCTATCCCTCTTTATATA ${\tt GCGCACAGCATTCCGAGTTTACAGATTTTTACAGATACCAA} {\color{red} {\bf ATG}} {\tt GAAGGCGAGAGCAGAACAGCCTGCCTGGT}$ TCCATCAGCCCTGGCGCCCAGGCGCATCTGACTCGGCACCCCTGCAGGCACCATGGCCCAGAGCCGGGTGCTGC TGCTCCTGCTGCTGCCGCCACAGCTGCACCTGGGACCTGTGCTTGCCGTGAGGGCCCCAGGATTTGGCCGAA GTGGCGGCCACAGCCTGAGCCCCGAAGAGAACGAATTTGCGGAGGAGGAGCCGGTGCTGGTACTGAGCCCTGAGG AGCCCGGGCCTGGCCCAGCCGCGGTCAGCTGCCCCCGAGACTGTGCCTGTTCCCAGGAGGGCGTCGTGGACTGTG TGGAAAAGATCTACCCTGAGGAGCTCTCCCGGCTGCACCGGCTGGAGACACTGAACCTGCAAAACAACCGCCTGA $\tt CTTCCCGAGGGGCTCCCAGAGAGGCGTTTGAGCATCTGACCAACCTCAATTACCTGTACTTGGCCAATAACAAGC$ TGACCTTGGCACCCGCTTCCTGCCAAACGCCCTGATCAGTGTGGACTTTGCTGCCAACTATCTCACCAAGATCT ATGGGCTCACCTTTGGCCAGAAGCCAAACTTGAGGTCTGTGTACCTGCACAACAACAAGCTGGCAGACGCCGGGC TGCCGGACAACATGTTCAACGGCTCCAGCAACGTCGAGGTCCTCATCCTGTCCAGCAACTTCCTGCGCCACGTGC CCAAGCACCTGCCGCCTGCCCTGTACAAGCTGCACCTCAAGAACAAGCTGGAGAAGATCCCCCCGGGGGCCT CCTTCTGGAAGCTCTCCAGCCTGGAGTACCTGGATCTGTCCAGCAACAACCTGTCTCGGGTCCCAGCTGGGCTGC CGCGCAGCCTGGTGCTGCACTTGGAGAAGAACGCCATCCGGAGCGTGGACGCGAATGTGCTGACCCCCATCC GCACCCTCATGATCCTGCACAACCAGATCACAGGCATTGGCCGCGAAGACTTTGCCACCACCTACTTCCTGGAGG GCTCGCTGGACCTGTCGGGCAACCGGCTGCACACGCTGCCACCTGGGCTGCCTCGAAATGTCCATGTGCTGAAGG TCAAGCGCAATGAGCTGCCTTGGCACGAGGGGGCGCTGGCGGGCATGGCTCAGCTGCGTGAGCTGTACCTCA TCGCCGGGAATCAGCTCACAGAGATCCCCGAGGGGGCTCCCCGAGTCACTTGAGTACCTGTACCTGCAGAACAACA AGATTAGTGCGGTGCCCGCCAATGCCTTCGACTCCACGCCCAACCTCAAGGGGATCTTTCTCAGGTTTAACAAGC TGGCTGTGGGCTCCGTGGTGGACAGTGCCTTCCGGAGGCTGAAGCACCTGCAGGTCTTGGACATTGAAGGCAACT AGGAAGAGAACAAGATGACAAGGTGATGCAGATGTGACCTAGGATGATGGACCGCCGGACTCTTTTCTGCA GCACACGCCTGTGTGCTGTGAGCCCCCCACTCTGCCGTGCTCACACAGACACCCCAGCTGCACACATGAGGCATCCCACATGACACGGGCTGACACAGTCTCATATCCCCACCCCTTCCCACGGCGTGTCCCACGGCCAGACACATGC GGAACTCACAAAAGCTGGCTTTTATTCCTTTCCCATCCTATGGGGACAGGAGCCTTCAGGACTGCTGGCCTGGCC CAGGCACTTTTCCAATGGGCAAGCCCAGTGGAGGCAGGATGGGAGAGCCCCCTGGGTGCTGCTGGGGCCTTGGGG

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FIGURE 370

MEGEEAEQPAWFHQPWRPGASDSAPPAGTMAQSRVLLLLLLLPPQLHLGPVLAVRAPGFGRSG
GHSLSPEENEFAEEEPVLVLSPEEPGPGPAAVSCPRDCACSQEGVVDCGGIDLREFPGDLPEH
TNHLSLQNNQLEKIYPEELSRLHRLETLNLQNNRLTSRGLPEKAFEHLTNLNYLYLANNKLTL
APRFLPNALISVDFAANYLTKIYGLTFGQKPNLRSVYLHNNKLADAGLPDNMFNGSSNVEVLI
LSSNFLRHVPKHLPPALYKLHLKNNKLEKIPPGAFSELSSLRELYLQNNYLTDEGLDNETFWK
LSSLEYLDLSSNNLSRVPAGLPRSLVLLHLEKNAIRSVDANVLTPIRSLEYLLLHSNQLREQG
IHPLAFQGLKRLHTVHLYNNALERVPSGLPRRVRTLMILHNQITGIGREDFATTYFLEELNLS
YNRITSPQVHRDAFRKLRLLRSLDLSGNRLHTLPPGLPRNVHVLKVKRNELAALARGALAGMA
QLRELYLTSNRLRSRALGPRAWVDLAHLQLLDIAGNQLTEIPEGLPESLEYLYLQNNKISAVP
ANAFDSTPNLKGIFLRFNKLAVGSVVDSAFRRLKHLQVLDIEGNLEFGDISKDRGRLGKEKEE
EEEEEEEEEEE

Important features:

Signal sequence:

amino acids 1-48

N-glycosylation site.

amino acids 243-247, 310-314, 328-332, 439-443

Casein kinase II phosphorylation site.

amino acids 68-72, 84-88, 246-250, 292-296, 317-321, 591-595

N-myristoylation site.

amino acids 19-25, 107-113, 213-219, 217-223, 236-242, 335-341, 477-483, 498-502, 539-545, 548-554

Leucine zipper pattern.

amino acids 116-138, 251-273, 258-280, 322-344, 464-486, 471-493, 535-557

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FIGURE 371

CACTTTCTCCTCTCTTTACTTTCGAGAAACCGCGCTTCCGCTTCTGGTCGCAGAGACCTCGGAGACCGCG CCGGGGAGACGGAGGTGCTGTGGGTGGGGGGGACCTGTGGCTGCTCGTACCGCCCCCACCCTCCTCTTCTGCAC TGCCGTCCTCCGGAAGACCTTTTCCCCTGCTCTGTTTCCTTCACCGAGTCTGTGCATCGCCCCGGACCTGGCCGG GAAG<u>ATG</u>GGCTCCCGTGGACAGGGACTCTTGCTGGCGTACTGCCTCCTTGCCTTTGCCTCTGGCCTGGTCCT GAGTCGTGTGCCCCATGTCCAGGGGGAACAGCAGGAGTGGGAGGGGACTGAGGAGCTGCCGTCGCCTCCGGACCA TGCCGAGAGGGCTGAAGAACATGAAAAATACAGGCCCAGTCAGGACCAGGGGCTCCCTGCTTCCCGGTGCTT GCGCTGCTGTGACCCCGGTACCTCCATGTACCCGGCGACCGCCGTGCCCCAGATCAACATCACTATCTTGAAAGG GGAGAAGGGTGACCGCGGAGATCGAGGCCTCCAAGGGAAATATGGCAAAACAGGCTCAGCAGGGGCCAGGGGCCA CACTGGACCCAAAGGGCAGAAGGGCTCCATGGGGGGCCCCTGGGGAGCGGTGCAAGAGCCACTACGCCGCCTTTTC GGTGGCCGGAAGAAGCCCATGCACAGCAACCACTACTACCAGACGGTGATCTTCGACACGGAGTTCGTGAACCT CTACGACCACTTCAACATGTTCACCGGCAAGTTCTACTGCTACGTGCCCGGCCTCTACTTCTTCAGCCTCAACGT GCACACCTGGAACCAGAAGGAGACCTACCTGCACATCATGAAGAACGAGGAGGAGGTGGTGATCTTGTTCGCGCA GGTGGGCGACCACCATCATGCAAAGCCAGAGCCTGATGCTGGAGCTGCGAGAGCAGGACCAGGTGTGGGTACG CCTCTACAAGGGCGAACGTGAGAACGCCATCTTCAGCGAGGAGCTGGACACCTACATCACCTTCAGTGGCTACCT GGTCAAGCACGCCACCGAGCCCTAGCTGGCCGGCCACCTCCTTTCCTCTCGCCACCTTCCACCCCTGCGCTGTGC TGACCCCACCGCCTCTTCCCCGATCCCTGGACTCCGACTCCCTGGCTTTGGCATTCAGTGAGACGCCCTGCACAC ACAGAAAGCCAAAGCGATCGGTGCTCCCAGATCCCGCAGCCTCTGGAGAGAGCTGACGGCAGATGAAATCACCAG GGCGGGGCACCCGCGAGAACCCTCTGGGACCTTCCGCGGCCCTCTCTGCACACATCCTCAAGTGACCCCGCACGG CGAGACGCGGGTGGCGGCAGGGCGTCCCAGGGTGCGGCACCGCGGCTCCAGTCCTTGGAAATAATTAGGCAAATT CCTGCTGGCTCCCAAGAGAGAGCCCTTTTCAGTTGAGACTCTGCTTAAGAGAAGATCCAAAGTTAAAGCTCTGGG GTCAGGGGAGGGCCGGGGCAGGAAACTACCTCTGGCTTAATTCTTTTAAGCCACGTAGGAACTTTCTTGAGGG ATAGGTGGACCCTGACATCCCTGTGGCCTTGCCCAAGGGCTCTGCTGGTCTTTCTGAGTCACAGCTGCGAGGTGA TGGGGGCTGGGGCCCCAGGCGTCAGCCTCCCAGAGGGACAGCTGAGCCCCCTGCCTTGGCTCCAGGTTGGTAGAA GCAGCCGAAGGGCTCCTGACAGTGGCCAGGGACCCCTGGGTCCCCCAGGCCTGCAGATGTTTCTATGAGGGGCAG AGCTCCTTGGTACATCCATGTGTGGCTCTGCTCCACCCCTGTGCCACCCCAGAGCCCTGGGGGGTGGTCTCCATG CCTGCCACCCTGGCATCGGCTTTCTGTGCCGCCTCCCACACAAATCAGCCCCAGAAGGCCCCGGGGCCTTGGCTT CTGTTTTTTATAAAACACCTCAAGCAGCACTGCAGTCTCCCATCTCCTCGTGGGCTAAGCATCACCGCTTCCACG TGTGTTGTGTTGGCAGCAGGCTGATCCAGACCCCTTCTGCCCCCACTGCCCTCATCCAGGCCTCTGACCA GTAGCCTGAGAGGGGCTTTTTCTAGGCTTCAGAGCAGGGGAGAGCTGGAAGGGGCTAGAAAGCTCCCGCTTGTCT GTTTCTCAGGCTCCTGTGAGCCTCAGTCCTGAGACCAGAGTCAAGAGGAAGTACACGTCCCAATCACCCGTGTCA GGATTCACTCTCAGGAGCTGGCTGGCAGGAGAGGCAATAGCCCCTGTGGCAATTGCAGGACCAGCTGGAGCAGGG TTGCGGTGTCTCCACGGTGCTCTCGCCCTGCCCATGGCCACCCCAGACTCTGATCTCCAGGAACCCCATAGCCCC TTCCTTCCCCCCATCCCCACCTGGTTTTGACTAATCCTGCTTCCCTCTCTGGGCCTGGCTGCCGGGATCTGGGG TCCCTAAGTCCCTCTCTTTAAAGAACTTCTGCGGGTCAGACTCTGAAGCCGAGTTGCTGTGGGCGTGCCCGGAAG CAGAGCGCCACACTCGCTGCTTAAGCTCCCCCAGCTCTTTCCAGAAAACATTAAACTCAGAATTGTGTTTTCAA

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FIGURE 372

MGSRGQGLLLAYCLLLAFASGLVLSRVPHVQGEQQEWEGTEELPSPPDHAERAEEQHEKYRPS
QDQGLPASRCLRCCDPGTSMYPATAVPQINITILKGEKGDRGDRGLQGKYGKTGSAGARGHTG
PKGQKGSMGAPGERCKSHYAAFSVGRKKPMHSNHYYQTVIFDTEFVNLYDHFNMFTGKFYCYV
PGLYFFSLNVHTWNQKETYLHIMKNEEEVVILFAQVGDRSIMQSQSLMLELREQDQVWVRLYK
GERENAIFSEELDTYITFSGYLVKHATEP

Important features:

Signal sequence.

amino acids 1-25

N-glycosylation site.

amino acids 93-97

N-myristoylation sites.

amino acids 7-13, 21-27, 67-73, 117-123, 129-135

Amidation site.

amino acids 150-154

Cell attachment sequence.

amino acids 104-107

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FIGURE 373

CGGAGTGGTGCGCCAACGTGAGAGGAAACCCGTGCGCGGCTGCGCTTTCCTGTCCCCAAGCCG TTCTAGACGCGGGAAAA**ATG**CTTTCTGAAAGCAGCTCCTTTTTGAAGGGTGTGATGCTTGGAA GCATTTTCTGTGCTTTGATCACTATGCTAGGACACATTAGGATTGGTCATGGAAATAGAATGC ACCACCATGAGCATCATCACCTACAAGCTCCTAACAAAGAAGATATCTTGAAAATTTCAGAGG ATGAGCGCATGGAGCTCAGTAAGAGCTTTCGAGTATACTGTATTATCCTTGTAAAACCCAAAG ATGTGAGTCTTTGGGCTGCAGTAAAGGAGACTTGGACCAAACACTGTGACAAAGCAGAGTTCT TCAGTTCTGAAAATGTTAAAGTGTTTGAGTCAATTAATATGGACACAAATGACATGTGGTTAA TGATGAGAAAAGCTTACAAATACGCCTTTGATAAGTATAGAGACCAATACAACTGGTTCTTCC TTGCACGCCCCACTACGTTTGCTATCATTGAAAACCTAAAGTATTTTTTGTTAAAAAAAGGATC CATCACAGCCTTTCTATCTAGGCCACACTATAAAATCTGGAGACCTTGAATATGTGGGTATGG AAGGAGGAATTGTCTTAAGTGTAGAATCAATGAAAAGACTTAACAGCCTTCTCAATATCCCAG AAAAGTGTCCTGAACAGGGAGGGATGATTTGGAAGATATCTGAAGATAAACAGCTAGCAGTTT GCCTGAAATATGCTGGAGTATTTGCAGAAAATGCAGAAGATGCTGATGGAAAAGATGTATTTA ATACCAAATCTGTTGGGCTTTCTATTAAAGAGGCAATGACTTATCACCCCAACCAGGTAGTAG TGATGTATGGGGTATACCGCCTTAGGGCATTTGGGCATATTTTCAATGATGCATTGGTTTTCT TACCTCCAAATGGTTCTGACAATGAC**TGA**GAAGTGGTAGAAAAGCGTGAATATGATCTTTGTA TAGGACGTGTGTCATTATTTGTAGTAGTAACTACATATCCAATACAGCTGTATGTTTCTT TTTCTTTTCTAATTTGGTGGCACTGGTATAACCACACATTAAAGTCAGTAGTACATTTTTAAA TGAGGGTGGTTTTTTTCTTTAAAACACATGAACATTGTAAATGTGTTGGAAAGAAGTGTTTTA AGAATAATATTTTGCAAATAAACTATTAATAAATATTTATATGTGATAAATTCTAAATTATGA ACATTAGAAATCTGTGGGGCACATATTTTTGCTGATTGGTTAAAAAATTTTAACAGGTCTTTA GCGTTCTAAGATATGCAAATGATATCTCTAGTTGTGAATTTGTGATTAAAGTAAAACTTTTAG CTGTGTGTTCCCTTTACTTCTAATACTGATTTATGTTCTAAGCCTCCCCAAGTTCCAATGGAT TTGCCTTCTCAAAATGTACAACTAAGCAACTAAAGAAAATTAAAGTGAAAGTTGAAAAAT

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FIGURE 374

MLSESSSFLKGVMLGSIFCALITMLGHIRIGHGNRMHHHEHHHLQAPNKEDILKISEDERMELSKSFRVYCIILV KPKDVSLWAAVKETWTKHCDKAEFFSSENVKVFESINMDTNDMWLMMRKAYKYAFDKYRDQYNWFFLARPTTFAI IENLKYFLLKKDPSQPFYLGHTIKSGDLEYVGMEGGIVLSVESMKRLNSLLNIPEKCPEQGGMIWKISEDKQLAV CLKYAGVFAENAEDADGKDVFNTKSVGLSIKEAMTYHPNQVVEGCCSDMAVTFNGLTPNQMHVMMYGVYRLRAFG HIFNDALVFLPPNGSDND

Important features:

Signal sequence:

amino acids 1-33

N-glycosylation site.

amino acids 121-125, 342-346

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 319-323, 464-468

Casein kinase II phosphorylation site.

amino acids 64-132, 150-154, 322-326, 331-335, 368-372, 385-389, 399-403, 409-413, 473-477, 729-733, 748-752

Tyrosine kinase phosphorylation site.

amino acids 736-743

N-myristoylation site.

amino acids 19-25, 23-29, 136-142, 397-403, 441-447, 544-550, 558-564, 651-657, 657-663, 672-672

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 14-25

Cell attachment sequence.

amino acids 247-250

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FIGURE 375

GTTGTGTCCTTCAGCAAAACAGTGGATTTAAATCTCCTTGCACAAGCTTGAGAGCAACACAAT AAAAATC**ATG**AAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCACGGG GCTGGCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAA AGCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATTGACAA CCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGACAAGTG GTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCATCGAGATCCA GACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAGATTTCTTCAGATAT CTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACTGGTAGACCAGAGCCTAC AATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAGTGCAGTGCCTCCAATGACGTGGC CGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAACTATCCACCATACATTCCAGAAGCCAA GGGTACAGGTGTCCCCGTGGGACAAAAGGGGACACTGCAGTGTGAAGCCTCAGCAGTCCCCTC GGAAAACAGACCTTTCCTCTCAAAACTCATCTTCTTCAATGTCTCTGAACATGACTATGGGAA CTACACTTGCGTGGCCTCCAACAAGCTGGGCCACACCAATGCCAGCATCATGCTATTTGGTCC AGGCGCCGTCAGCGAGGTGAGCAACGGCACGTCGAGGAGGGCAGGCTGCGTCTGGCTGCCC TCTTCTGGTCTTGCACCTGCTTCTCAAATTT**TGA**TGTGAGTGCCACTTCCCCACCCGGGAAAG GCTGCCGCCACCACCACCACCACACACACAGCAATGGCAACACCGACAGCAACCAATCAGATA GAATACTTTGGGGGGAAAAGAGTTTTAAAAAAGAAATTGAAAATTGCCTTGCAGATATTTAGG TACAATGGAGTTTTCTTTTCCCAAACGGGAAGAACACAGCACACCCGGCTTGGACCCACTGCA AGCTGCATCGTGCAACCTCTTTGGTGCCAGTGTGGGCAAGGGCTCAGCCTCTCTGCCCACAGA GTGCCCCCACGTGGAACATTCTGGAGCTGGCCATCCCAAATTCAATCAGTCCATAGAGACGAA CAGAATGAGACCTTCCGGCCCAAGCGTGGCGCTGCGGGCACTTTGGTAGACTGTGCCACCACG

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FIGURE 376

MKTIQPKMHNSISWAIFTGLAALCLFQGVPVRSGDATFPKAMDNVTVRQGESATLRCTIDNRV
TRVAWLNRSTILYAGNDKWCLDPRVVLLSNTQTQYSIEIQNVDVYDEGPYTCSVQTDNHPKTS
RVHLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYLEIQ
GITREQSGDYECSASNDVAAPVVRRVKVTVNYPPYISEAKGTGVPVGQKGTLQCEASAVPSAE
FQWYKDDKRLIEGKKGVKVENRPFLSKLIFFNVSEHDYGNYTCVASNKLGHTNASIMLFGPGA
VSEVSNGTSRRAGCVWLLPLLVLHLLLKF

Important features:

Signal peptide:

amino acids 1-28

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FIGURE 377

CTTCTTTGAAAAGGATTATCACCTGATCAGGTTCTCTCTGCATTTGCCCCCTTTAGATTGTGAA TATGGCTTCCACACTCCAGCATCAGACATCCAGATCATATGGCTATTTGAGAGACCCCACACA ATGCCCAAATACTTACTGGGCTCTGTGAATAAGTCTGTGGTTCCTGACTTGGAATACCAACAC AAGTTCACCATGATGCCACCCAATGCATCTCTGCTTATCAACCCACTGCAGTTCCCTGATGAA GGCAATTACATCGTGAAGGTCAACATTCAGGGAAATGGAACTCTATCTGCCAGTCAGAAGATA GTGGAGTATGTGGGGAACATGACCCTGACATGCCATGTGGAAGGGGGCACTCGGCTAGCTTAC CAATGGCTAAAAAATGGGAGACCTGTCCACACCAGCTCCACCTACTCCTTTTCTCCCCAAAAC AATACCCTTCATATTGCTCCAGTAACCAAGGAAGACATTGGGAATTACAGCTGCCTGGTGAGG AACCCTGTCAGTGAAATGGAAAGTGATATCATTATGCCCATCATATATTATGGACCTTATGGA CTTCAAGTGAATTCTGATAAAGGGCTAAAAGTAGGGGAAGTGTTTACTGTTGACCTTGGAGAG GCCATCCTATTTGATTGTTCTGCTGATTCTCATCCCCCCAACACCTACTCCTGGATTAGGAGG ACTGACAATACTACATATATCATTAAGCATGGGCCTCGCTTAGAAGTTGCATCTGAGAAAGTA ACTCATTTCACAGTTATCATCACTTCCGTAGGACTGGAGAAGCTTGCACAGAAAGGAAAATCA TTGTCACCTTTAGCAAGTATAACTGGAATATCACTATTTTTGATTATATCCATGTGTCTTCTC ACAGAATACAGGAAAGCTCAAACATTTTCAGGCCATGAAGATGCTCTGGATGACTTCGGAATA TATGAATTTGTTGCTTTTCCAGATGTTTCTGGTGTTTCCAGGATTCCAAGCAGGTCTGTTCCA GCCTCTGATTGTGTATCGGGGCAAGATTTGCACAGTACAGTGTATGAAGTTATTCAGCACATC CCTGCCCAGCAAGACCATCCAGAG<u>TGA</u>ACTTTCATGGGCTAAACAGTACATTCGAGTGAA ATTCTGAAGAAACATTTTAAGGAAAAACAGTGGAAAAGTATATTAATCTGGAATCAGTGAAGA AACCAGGACCAACACCTCTTACTCATTATTCCTTTACATGCAGAATAGAGGCATTTATGCAAA TTGAACTGCAGGTTTTTCAGCATATACACAATGTCTTGTGCAACAGAAAAACATGTTGGGGAA ATATTCCTCAGTGGAGAGTCGTTCTCATGCTGACGGGGAGAACGAAAGTGACAGGGGTTTCCT CATAAGTTTTGTATGAAATATCTCTACAAACCTCAATTAGTTCTACTCTACACTTTCACTATC ATCAACACTGAGACTATCCTGTCTCACCTACAAATGTGGAAACTTTACATTGTTCGATTTTTC AGCAGACTTTGTTTTATTAAATTTTTTTTTTTTAGTGTTTAAGAATGCTAAATTTATGTTTCAATTTT ATTTCCAAATTTCTATCTTGTTATTTGTACAACAAAGTAATAAGGATGGTTGTCACAAAAACA AAACTATGCCTTCTCTTTTTTTCAATCACCAGTAGTATTTTTTGAGAAGACTTGTGAACACTT ATTCTGTTTTTGCTTTTAAAAAAAAAAAAAAA

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FIGURE 378

MWLKVFTTFLSFATGACSGLKVTVPSHTVHGVRGQALYLPVHYGFHTPASDIQIIWLFERPHTMPKYLLGSVNKS
VVPDLEYQHKFTMMPPNASLLINPLQFPDEGNYIVKVNIQGNGTLSASQKIQVTVDDPVTKPVVQIHPPSGAVEY
VGNMTLTCHVEGGTRLAYQWLKNGRPVHTSSTYSFSPQNNTLHIAPVTKEDIGNYSCLVRNPVSEMESDIIMPII
YYGPYGLQVNSDKGLKVGEVFTVDLGEAILFDCSADSHPPNTYSWIRRTDNTTYIIKHGPRLEVASEKVAQKTMD
YVCCAYNNITGRQDETHFTVIITSVGLEKLAQKGKSLSPLASITGISLFLIISMCLLFLWKKYQPYKVIKQKLEG
RPETEYRKAQTFSGHEDALDDFGIYEFVAFPDVSGVSRIPSRSVPASDCVSGQDLHSTVYEVIQHIPAQQQDHPE

Important features:

Signal sequence:

amino acids 1-18

Transmembrane domain:

amino acids 341-359

N-glycosylation site.

amino acids 73-77, 92-96, 117-121, 153-157, 189-193, 204-208, 276-280, 308-312

Casein kinase II phosphorylation site.

amino acids 129-133, 198-202, 214-218, 388-392, 426-430, 433-437

Tyrosine kinase phosphorylation site.

amino acids 272-280

N-myristoylation site.

amino acids 15-21, 19-25, 118-124, 163-167, 203-209, 231-237, 239-245

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 7-18

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FIGURE 379

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FIGURE 380

MYRHKNSWRLGLKYPPSSKEETQVPKTLISGLPGRKSSSRVGEKLQSAHKMPLSPGLLLLLLS GATATAALPLEGGPTGRDSEHMQEAAGIRKSSLLTFLAWWFEWTSQASAGPLIGEEAREVARR QEGAPPQQSARRDRMPCRNFFWKTFSSCK

Important features:

Transmembrane domain:

amino acids 51-69

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 35-39, 92-96

N-myristoylation sites.

amino acids 64-70, 75-81, 90-96

Amidation site.

amino acids 33-37

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FIGURE 381

CGGCCGGCGGGGGAACCGGGCGGATTCCTCGCGCGTCAAACCACCTGATCCCATAAAACATTC ATCCTCCGGCGGCCCGCGCTGCGAGCGCCCCGCCAGTCCGCGCCGCCGCCGCCCTCGCCCTG TGCGCCCTGCGCGCCCCGCGCCCCGAGCCCAGCCAGAGCCGGGCGGAGCGGAGCG CGCCGAGCCTCGTCCCGCGGCCGGGCCGGGCCGGCCGTAGCGGCGCCCTGGATGCGGAC CCGGCCGCGGGGAGACGGCCCCGCCCCGAAACGACTTTCAGTCCCCGACGCGCCCCGCCCA ACCCCTACG<u>ATG</u>AAGAGGGCGTCCGCTGGAGGGAGCCGGCTGCTGGCATGGGTGCTGTGGCTG CAGGCCTGGCAGGTGGCAGCCCCATGCCCAGGTGCCTGCGTATGCTACAATGAGCCCAAGGTG AACCTCACCATCCTGTGGCTGCACTCGAATGTGCTGGCCCGAATTGATGCGGCTGCCTTCACT GGCCTGGCCCTCCTGGAGCAGCTGGACCTCAGCGATAATGCACAGCTCCGGTCTGTGGACCCT GCCACATTCCACGGCCTGGGCCGCCTACACACGCTGCACCTGGACCGCTGCGGCCTGCAGGAG CTGGGCCCGGGGCTGTTCCGCGGCCTGGCTGCCCTGCAGTACCTCTACCTGCAGGACAACGCG CTGCAGGCACTGCTGATGACACCTTCCGCGACCTGGGCAACCTCACACACCTCTTCCTGCAC GGCAACCGCATCTCCAGCGTGCCCGAGCGCGCCTTCCGTGGGCTGCACAGCCTCGACCGTCTC CTACTGCACCAGAACCGCGTGGCCCATGTGCACCCGCATGCCTTCCGTGACCTTGGCCGCCTC ATGACACTCTATCTGTTTGCCAACAATCTATCAGCGCTGCCCACTGAGGCCCTGGCCCCCTG CGTGCCCTGCAGTACCTGAGGCTCAACGACAACCCCTGGGTGTGACTGCCGGGCACGCCCA CTCTGGGCCTGCAGAAGTTCCGCGGCTCCTCCTCCGAGGTGCCCTGCAGCCTCCCGCAA CGCCTGGCTGGCCGTGACCTCAAACGCCTAGCTGCCAATGACCTGCAGGGCTGCGCTGTGGCC ACCGGCCCTTACCATCCCATCTGGACCGGCAGGGCCACCGATGAGGAGCCGCTGGGGCTTCCC AAGTGCTGCCAGCCAGATGCCGCTGACAAGGCCTCAGTACTGGAGCCTGGAAGACCAGCTTCG GCAGGCAATGCGCTGAAGGGACGCGTGCCGCCCGGTGACAGCCCGCCGGGCAACGGCTCTGGC CCACGGCACATCAATGACTCACCCTTTGGGACTCTGCCTGGCTCTGCTGAGCCCCCGCTCACT GCAGTGCGGCCCGAGGCTCCGAGCCACCAGGGTTCCCCACCTCGGGCCCTCGCCGGAGGCCA GGCGGGACTGGTGACTCAGAAGGCTCAGGTGCCCTACCCAGCCTCACCTGCAGCCTCACCCCC CTGGGCCTGGCGCTGTGGACAGTGCTTGGGCCCTGC<u>TGA</u>CCCCCAGCGGACACAAGA CCCATCTCCACCCCATCATGTTTACAGGGTTCGGCGGCAGCGTTTGTTCCAGAACGCCGCCTC CCACCCAGATCGCGGTATATAGAGATATGCATTTTATTTTACTTGTGTAAAAATATCGGACGA CGTGGAATAAAGAGCTCTTTTCTTAAAAAAA

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FIGURE 382

MKRASAGGSRLLAWVLWLQAWQVAAPCPGACVCYNEPKVTTSCPQQGLQAVPVGIPAASQRIF
LHGNRISHVPAASFRACRNLTILWLHSNVLARIDAAAFTGLALLEQLDLSDNAQLRSVDPATF
HGLGRLHTLHLDRCGLQELGPGLFRGLAALQYLYLQDNALQALPDDTFRDLGNLTHLFLHGNR
ISSVPERAFRGLHSLDRLLLHQNRVAHVHPHAFRDLGRLMTLYLFANNLSALPTEALAPLRAL
QYLRLNDNPWVCDCRARPLWAWLQKFRGSSSEVPCSLPQRLAGRDLKRLAANDLQGCAVATGP
YHPIWTGRATDEEPLGLPKCCQPDAADKASVLEPGRPASAGNALKGRVPPGDSPPGNGSGPRH
INDSPFGTLPGSAEPPLTAVRPEGSEPPGFPTSGPRRPGCSRKNRTRSHCRLGQAGSGGGT
GDSEGSGALPSLTCSLTPLGLALVLWTVLGPC

Important features:

Signal peptide:

amino acids 1-26

Leucine zipper pattern.

amino acids 135-156

Glycosaminoglycan attachment site.

amino acids 436-439

N-glycosylation site.

amino acids 82-85, 179-183, 237-240, 372-375 and 423-426

VWFC domain

amino acids 411-425

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FIGURE 383

TTCGTGACCCTTGAGAAAAGAGTTGGTGGTAAATGTGCCACGTCTTCTAAGAAGGGGGGAGTCCTGAACTTGTCTG AAGCCCTTGTCCGTAAGCCTTGAACTACGTTCTTAAATCTATGAAGTCGAGGGACCTTTCGCTGCTTTTGTAGGG ACTTCTTTCCTTGCTTCAGCAAC**ATG**AGGCTTTTCTTGTGGAACGCGGTCTTGACTCTGTTCGTCACTTCTTTGA TTGGGGCTTTGATCCCTGAACCAGAAGTGAAAATTGAAGTTCTCCAGAAGCCATTCATCTGCCATCGCAAGACCA AAGGAGGGGATTTGATGTTGGTCCACTATGAAGGCTACTTAGAAAAGGACGGCTCCTTATTTCACTCCACTCACA AACATAACAATGGTCAGCCCATTTGGTTTACCCTGGGCATCCTGGAGGCTCTCAAAGGTTGGGACCAGGGCTTGA AAGGAATGTGTGTAGGAGAGAGAGAAAGCTCATCATTCCTCCTGCTCTGGGCTATGGAAAAGAAGGAAAAGGTA AAATTCCCCCAGAAAGTACACTGATATTTAATATTGATCTCCTGGAGATTCGAAATGGACCAAGATCCCATGAAT CATTCCAAGAAATGGATCTTAATGATGACTGGAAACTCTCTAAAGATGAGGTTAAAGCATATTTAAAGAAGGAGGT TTGAAAAACATGGTGCGGTGGTGAATGAAAGTCATCATGATGCTTTGGTGGAGGATATTTTTGATAAAGAAGATG AAGACAAAGATGGGTTTATATCTGCCAGAGAATTTACATATAAACACGATGAGTTA**TAG**AGATACATCTACCCTT $\tt CTTTCTGATAAGTTATTGGGAAGAAAAGCTAATTGGTCTTTGAATAGAAGACTTCTGGACAATTTTTCACTTTC$ ACAGATATGAAGCTTTGTTTTACTTTCTCACTTATAAATTTAAAATGTTGCAACTGGGAATATACCACGACATGA GACCAGGTTATAGCACAAATTAGCACCCTATATTTCTGCTTCCCTCTATTTTCTCCAAGTTAGAGGTCAACATTT GAAAAGCCTTTTGCAATAGCCCAAGGCTTGCTATTTTCATGTTATAATGAAATAGTTTATGTGTAACTGGCTCTG AGTCTCTGCTTGAGGACCAGAGGAAAATGGTTGTTGGACCTGACTTGTTAATGGCTACTGCTTTACTAAGGAGAT GTGCAATGCTGAAGTTAGAAACAAGGTTAATAGCCAGGCATGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGA GGCTGAGGCGGGCGGATCACCTGAGGTTGGGAGTTCGAGACCAGCCTGACCAACACGGAGAAACCCTATCTCTAC TAAAAATACAAAGTAGCCCGGCGTGGTGATGCGTGCCTGTAATCCCAGCTACCCAGGAAGGCTGAGGCGGCAGAA TCACTTGAACCCGAGGCCGAGGTTGCGGTAAGCCGAGATCACCTNCAGCCTGGACACTCTGTCTCGAAAAAAAGAA AAGAACACGGTTAATACCATATNAATATGTATGCATTGAGACATGCTACCTAGGACTTAAGCTGATGAAGCTTGG CTCCTAGTGATTGGTGGCCTATTATGATAAATAGGACAAATCATTTATGTGTGAGTTTCTTTGTAATAAAATGTA TCAATATGTTATAGATGAGGTAGAAAGTTATATTTATATTCAATATTTACTTCTTAAGGCTAGCGGAATATCCTT CCTGGTTCTTTAATGGGTAGTCTATAGTATATTATACTACAATAACATTGTATCATAAGATAAAGTAGTAAACCA GTCTACATTTTCCCATTTCTGTCTCATCAAAAACTGAAGTTAGCTGGGTGTGGTGGCTCATGCCTGTAATCCCAG CACTTTGGGGGCCAAGGGGGGGGATCACTTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCT TGTCTCTACTAAAAATTACAAAAATTAGCCAGGCGTGGTGGTGCACACCTGTAGTCCCAGCTACTCGGGAGGCTGA GACAGGAGATTTGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCAAGATTGTGCCACTGCACTCCAGCCTGGG TCCTGGATTTT

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FIGURE 384

MRLFLWNAVLTLFVTSLIGALIPEPEVKIEVLQKPFICHRKTKGGDLMLVHYEGYLEKDGSLF HSTHKHNNGQPIWFTLGILEALKGWDQGLKGMCVGEKRKLIIPPALGYGKEGKGKIPPESTLI FNIDLLEIRNGPRSHESFQEMDLNDDWKLSKDEVKAYLKKEFEKHGAVVNESHHDALVEDIFD KEDEDKDGFISAREFTYKHDEL

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 176-179

Casein kinase II phosphorylation site.

amino acids 143-146, 156-159, 178-181 and 200-203

Endoplasmic reticulum targeting sequence.

amino acids 208-211

FKBP-type peptidyl-prolyl cis-trans isomerase

amino acids 78-114 and 118-131

EF-hand calcium-binding domain.

amino acids 191-203, 184-203 and 140-159

S-100/ICaBP type calcium binding domain

amino acids 183-203

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FIGURE 385

CTCCCACGGTGTCCAGCGCCCAGAATGCGGCTTCTGGTCCTGCTATGGGGTTGCCTGCTGCTC CCAGGTTATGAAGCCCTGGAGGGCCCAGAGGAAATCAGCGGGTTCGAAGGGGACACTGTGTCC CTGCAGTGCACCTACAGGGAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGTGGG ATCCTCTTCTCTCGCTGCTCTGGCACCATCTATGCAGAAGAAGAAGACCAGGAGACAATGAAG GGCAGGGTGTCCATCCGTGACAGCCGCCAGGAGCTCTCGCTCATTGTGACCCTGTGGAACCTC ACCCTGCAAGACGCTGGGGAGTACTGGTGTGGGGTCGAAAAACGGGGCCCCGATGAGTCTTTA CTGATCTCTCTGTTCGTCTTTCCAGGACCCTGCTGTCCTCCCCTCCCCTTCTCCCACCTTCCAG CCTCTGGCTACAACACGCCTGCAGCCCAAGGCAAAAGCTCAGCAAACCCAGCCCCCAGGATTG ACTTCTCCTGGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGGGCTGAGGCC CCTCCATTGCCAGGGACTTCCCAGTACGGGCACGAAAGGACTTCTCAGTACACAGGAACCTCT CCTCACCCAGCGACCTCTCCTCCTGCAGGGAGCTCCCGCCCCCCATGCAGCTGGACTCCACC TCAGCAGAGGACACCAGTCCAGCTCTCAGCAGTGGCAGCTCTAAGCCCAGGGTGTCCATCCCG ATGGTCCGCATACTGGCCCCAGTCCTGGTGCTGAGCCTTCTGTCAGCCGCAGGCCTGATC GCCTTCTGCAGCCACCTGCTCCTGTGGAGAAAGGAAGCTCAACAGGCCACGGAGACACAGAGG AACGAGAAGTTCTGGCTCTCACGCTTGACTGCGGAGGAAAAGGAAGCCCCTTCCCAGGCCCCT GAGGGGGACGTGATCTCGATGCCTCCCCTCACACATCTGAGGAGGAGCTGGGCTTCTCGAAG TGGATCAGCACCGATTCCCGAAAGCTTTCCACCTCAGCCTCAGAGTCCAGCTGCCCGGACTCC AGGGCTCTCCCCACCCTCCCCAGGCTCTCCTCTTGCATGTTCCAGCCTGACCTAGAAGCGTTT GTCAGCCCTGGAGCCCAGAGCGGTGGCCTTGCTCTTCCGGCTGGAGACTGGGACATCCCTGAT AGGTTCACATCCCTGGGCAGAGTACCAGGCTGCTGACCCTCAGCAGGGCCAGACAAGGCTCAG TGGATCTGGTCTGAGTTTCAATCTGCCAGGAACTCCTGGGCCTCATGCCCAGTGTCGGACCCT CGGTCTCCTGCATCAGCTGGTGATGAAGAGGAGCATGCTGGGGTGAGACTGGGATTCTGGCTT CTCTTTGAACCACCTGCATCCAGCCCTTCAGGAAGCCTGTGAAAAACGTGATTCCTGGCCCCA CCAAGACCCACCAAAACCATCTCTGGGCTTGGTGCAGGACTCTGAATTCTAACAATGCCCAGT GACTGTCGCACTTGAGTTTGAGGGCCAGTGGGCCTGATGAACGCTCACACCCCTTCAGCTTAG GATCCACGTGGGGACTCCCCTGAGGCCTGCTAAGTCCAGGCCTTGGTCAGGTCAGGTGCACAT TGCAGGATAAGCCCAGGACCGGCACAGAAGTGGTTGCCTTTNCCATTTGCCCTCCCTGGNCCA TTACTTGCCTATGGGTTCTGGTGGCTAGAGAGAAAAGTAGAAAACCAGAGTGCACGTAGGTGT CTAACACAGAGGAGAGTAGGAACAGGGCGGATACCTGAAGGTGACTCCGAGTCCAGCCCCCTG ATTGTTTTTTAAGACAGAATCTCGTGCTGCTGCCCAGGCTGGAGTGCAGTGGCACGATCTGCA AACTCCGCCTCCTGGGTTCAAGTGATTCTTCTGCCTCAGCCTCCCGAGTAGCTGGGATTACAG GCACGCACCACCACCTGGCTAATTTTTGTACTTTTAGTAGAGATGGGGTTTCACCATGTTG GCCAGGCTGGTCTTGAACTCCTGACCTCAAATGAGCCTCCTGCTTCAGTCTCCCAAATTGCCG GGATTACAGGCATGAGCCACTGTGTCTGGCCCTATTTCCTTTAAAAAGTGAAATTAAGAGTTG ACATAATTTGCCGGTGTTCTTTTTACAGAGCAATTATCTTGTATATACAACTTTGTATCCTGC CTTTTCCACCTTATCGTTCCATCACTTTATTCCAGCACTTCTCTGTGTTTTTACAGACCTTTTT

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FIGURE 386

MRLLVLLWGCLLLPGYEALEGPEEISGFEGDTVSLQCTYREELRDHRKYWCRKGGILFSRCSG
TIYAEEEGQETMKGRVSIRDSRQELSLIVTLWNLTLQDAGEYWCGVEKRGPDESLLISLFVFP
GPCCPPSPSPTFQPLATTRLQPKAKAQQTQPPGLTSPGLYPAATTAKQGKTGAEAPPLPGTSQ
YGHERTSQYTGTSPHPATSPPAGSSRPPMQLDSTSAEDTSPALSSGSSKPRVSIPMVRILAPV
LVLLSLLSAAGLIAFCSHLLLWRKEAQQATETQRNEKFWLSRLTAEEKEAPSQAPEGDVISMP
PLHTSEEELGFSKFVSA

Important features:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 248-269

N-glycosylation site.

amino acids 96-99

Fibrinogen beta and gamma chains C-terminal domain.

amino acids 104-113

Ig like V-type domain:

amino acids 13-128

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FIGURE 387

GCTGCAGCCACCTCGCGCGCACCCCGAGGCCCCGCCCAGCTCGCCCGAGGTCCGTCGGAGG CGCCCGGCCCCCGGAGCCAAGCAGCAACTGAGCGGGAAGCGCCCGCGTCCGGGGATCGGG <u>ATG</u>TCCCTCCTTCTCCTCTTGCTAGTTTCCTACTATGTTGGAACCTTGGGGACTCACACT GAGATCAAGAGAGTGGCAGAGGAAAAGGTCACTTTGCCCTGCCACCATCAACTGGGGCTTCCA GAAAAAGACACTCTGGATATTGAATGGCTGCTCACCGATAATGAAGGGAACCAAAAAGTGGTG ATCACTTACTCCAGTCGTCATGTCTACAATAACTTGACTGAGGAACAGAAGGGCCGAGTGGCC TTTGCTTCCAATTTCCTGGCAGGAGATGCCTCCTTGCAGATTGAACCTCTGAAGCCCAGTGAT GAGGGCCGGTACACCTGTAAGGTTAAGAATTCAGGGCCGCTACGTGTGGAGCCATGTCATCTTA GACCTGACTTTGCAGTGTGAGTCATCCTCTGGCACAGAGCCCATTGTGTATTACTGGCAGCGA ATCCGAGAGAAAGAGGGAGGATGAACGTCTGCCTCCCAAATCTAGGATTGACTACAACCAC CCTGGACGAGTTCTGCTGCAGAATCTTACCATGTCCTACTCTGGACTGTACCAGTGCACAGCA GGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCGAGTAACTGTACAGTATGTACAAAGCATC GGCATGGTTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTGATTTTCCTCTTGGTG TGGCTGCTAATCCGAAGGAAAGACAAAGAAGATATGAGGAAGAAGACACCTAATGAAATT CGAGAAGATGCTGAAGCTCCAAAAGCCCGTCTTGTGAAACCCAGCTCCTCTTCCTCAGGCTCT CGGAGCTCACGCTCTGGTTCTTCCTCCACTCGCTCCACAGCAAATAGTGCCTCACGCAGCCAG CGGACACTGTCAACTGACGCAGCACCCCAGCCAGGGCTGGCCACCCAGGCATACAGCCTAGTG GGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAGTCCACCATGCTAATCTGACCAAAGCAGAA ACCACACCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAAACGGTC<u>TGA</u>ATTACAATGGAC TTGACTCCCACGCTTTCCTAGGAGTCAGGGTCTTTGGACTCTTCTCGTCATTGGAGCTCAAGT CACCAGCCACAACCAGATGAGAGGTCATCTAAGTAGCAGTGAGCATTGCACGGAACAGATT CAGATGAGCATTTTCCTTATACAATACCAAACAAGCAAAAGGATGTAAGCTGATTCATCTGTA AAAAGGCATCTTATTGTGCCTTTAGACCAGAGTAAGGGAAAGCAGGAGTCCAAATCTATTTGT TGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTGAGGTGAATATACCTAAAACTTTTAAT GTGGGATATTTTGTATCAGTGCTTTGATTCACAATTTTCAAGAGGAAATGGGATGCTGTTTGT AAATTTTCTATGCATTTCTGCAAACTTATTGGATTATTAGTTATTCAGACAGTCAAGCAGAAC CCACAGCCTTATTACACCTGTCTACACCATGTACTGAGCTAACCACTTCTAAGAAACTCCAAA AAAGGAAACATGTGTCTTCTATTCTGACTTAACTTCATTTGTCATAAGGTTTGGATATTAATT TCAAGGGGAGTTGAAATAGTGGGAGATGGAGAAGAGTGAATGAGTTTCTCCCACTCTATACTA ATCTCACTATTTGTATTGAGCCCAAAATAACTATGAAAGGAGACAAAAATTTGTGACAAAGGA TTGTGAAGAGCTTTCCATCTTCATGATGTTATGAGGATTGTTGACAAACATTAGAAATATATA ATGGAGCAATTGTGGATTTCCCCTCAAATCAGATGCCTCTAAGGACTTTCCTGCTAGATATTT ATGTGAAACCAGAATTGCAAGACTGGGTGGACTAGAAAGGGAGATTAGATCAGTTTTCTCTTA ATATGTCAAGGAAGGTAGCCGGGCATGGTGCCAGGCACCTGTAGGAAAATCCAGCAGGTGGAG GTTGCAGTGAGCCGAGATTATGCCATTGCACTCCAGCCTGGGTGACAGAGCGGGACTCCGTCTC

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FIGURE 388

MSLLLLLLVSYYVGTLGTHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKVV
ITYSSRHVYNNLTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHVIL
KVLVRPSKPKCELEGELTEGSDLTLQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRIDYNH
PGRVLLQNLTMSYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLIFLLV
WLLIRRKDKERYEEEERPNEIREDAEAPKARLVKPSSSSSGSRSSRSGSSSTRSTANSASRSQ
RTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHANLTKAETTPSMIPSQSRAFQTV

Important freatures:

Signal sequence:

amino acids 1-16

Transmembrane domain:

amino acids 232-251

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FIGURE 389

GCGGCACCTGGAAGATGCGCCCATTGGCTGGTGGCCTGCTCAAGGTGGTGTTCGTGGTCTTCG CCTCCTTGTGTGCCTGGTATTCGGGGTACCTGCTCGCAGAGCTCATTCCAGATGCACCCCTGT CCAGTGCTGCCTATAGCATCCGCAGCATCGGGGAGAGGCCTGTCCTCAAAGCTCCAGTCCCCA AAAGGCAAAAATGTGACCACTGGACTCCCTGCCCATCTGACACCTATGCCTACAGGTTACTCA GCGGAGGTGGCAGAAGCAAGTACGCCAAAATCTGCTTTGAGGATAACCTACTTATGGGAGAAC AGCTGGGAAATGTTGCCAGAGGAATAAACATTGCCATTGTCAACTATGTAACTGGGAATGTGA CAGCAACACGATGTTTTGATATGTATGAAGGCGATAACTCTGGACCGATGACAAAGTTTATTC AGAGTGCTGCTCCAAAATCCCTGCTCTTCATGGTGACCTATGACGACGGAAGCACAAGACTGA ATAACGATGCCAAGAATGCCATAGAAGCACTTGGAAGTAAAGAAATCAGGAACATGAAATTCA GGTCTAGCTGGGTATTTATTGCAGCAAAAGGCTTGGAACTCCCTTCCGAAATTCAGAGAGAAA ${\tt AAGGCTGCATACCCAAAGAACGAAGC} \underline{{\tt TGA}} {\tt CACTGCAGGGTCCTGAGTAAATGTGTTCTGTATA}$ AACAAATGCAGCTGGAATCGCTCAAGAATCTTATTTTTCTAAATCCAACAGCCCATATTTGAT GAGTATTTTGGGTTTGTTAAACCAATGAACATTTGCTAGTTGTATCAAATCTTGGTACGCA AAATTCTTAAAAAAAAAA

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FIGURE 390

MRPLAGGLLKVVFVVFASLCAWYSGYLLAELIPDAPLSSAAYSIRSIGERPVLKAPVPKRQKC DHWTPCPSDTYAYRLLSGGGRSKYAKICFEDNLLMGEQLGNVARGINIAIVNYVTGNVTATRC FDMYEGDNSGPMTKFIQSAAPKSLLFMVTYDDGSTRLNNDAKNAIEALGSKEIRNMKFRSSWV FIAAKGLELPSEIQREKINHSDAKNNRYSGWPAEIQIEGCIPKERS

Important features:

Signal sequence.

amino acids 1-20

N-glycosylation sites.

amino acids 120-124, 208-212

Glycosaminoglycan attachment site.

amino acids 80-84

N-myristoylation sites.

amino acids 81-87, 108-114, 119-125

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FIGURE 391

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGTCGCCGGGAAAGGG AGGGAAGAAGGAAGGGCGGGCCGGCCCCTGCGCCCCCGCGCCCTCTGCGCCCCTGTCCGCCCCGGCCC GCCCTGGGCGGGGGGGAGCAGGCATGTCCCGCCCGGGGACCGCTACCCCAGCGCTGGCCCTGGTGCTCCTGGC AGTGACCCTGGCCGGGGTCGGAGCCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACGGGCAGGAGATCTGGAG GGAGTGGGAGCGCCCGCAGGAGCCCAGGCCGCCCAAGAGGCCCAAGCCCAAGAAAGCTCCCAAGAGGGGA GAAGTCGGCTCCGGAGCCGCCTCCACCAGGTAAACACAGCAACAAAAAAGTTATGAGAACCAAGAGCTCTGAGAA GGCTGCCAACGATGATCACAGTGTCCGTGTGGCCCGTGAAGATGTCAGAGAGTTGCCCACCTCTTGGTCTGGA AACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCCTGGGGGGCACATCGAGGGAG ACTCAACATCCAGGCGGGCATTAATGAAAATGATTTTTATGACGGAGCGTGGTGCGCGGGAAGAAATGACCTCCA GCAGTGGATTGAAGTGGATGCTCGGCGCCTGACCAGATTCACTGGTGTCATCACTCAAGGGAGGAACTCCCTCTG GCTGAGTGACTGGGTGACATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGTCACTGTTAAGAATGG ATCTGGAGACATGATATTTGAGGGAAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCTACCCGTCCCCATGGT GGCCCGCTACATCCGCATAAACCCTCAGTCCTGGTTTGATAATGGGAGCATCTGCATGAGAATGGAGATCCTGGG CTGCCCACTGCCAGATCCTAATAATTATTATCACCGCCGGAACGAGATGACCACCACTGATGACCTGGATTTTAA CAACATTGGAAAAAGCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATCACCCTGGGGAGCATGAAGT CGGTGAGCCCGAGTTCCACTACATCGCGGGGGCCCACGGCAATGAGGTGCTGGCCGGGAGCTGCTGCTGCTGCT GGTGCAGTTCGTGTGTCAGGAGTACTTGGCCCGGAATGCGCGCATCGTCCACCTGGTGGAGGAGACGCGGATTCA CGTCCTCCCTCAACCCCGATGGCTACGAGAAGGCCTACGAAGGGGGCTCGGAGCTGGGAGGCTGGTCCCT GGGACGCTGGACCCACGATGGAATTGACATCAACAACAACTTTCCTGATTTAAACACGCTGCTCTGGGAGGCAGA GGATCGACAGAATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCCTGAGTGGTTTCTGTCGGAAAATGC GGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCCCCTGGAAGACGCAGGAACACACCCCCAC CCCCGATGACCACGTGTTCCGCTGGCCTGCCTACTCCTATGCCTCCACACACCGCCTCATGACAGACGCCCGGAG GAGGGTGTGCCACACGGAGGACTTCCAGAAGGAGGAGGGCACTGTCAATGGGGCCTCCTGGCACACCGTCGCTGG AAGTCTGAACGATTTCAGCTACCTTCATACAAACTGCTTCGAACTGTCCATCTACGTGGGCTGTGATAAATACCC ACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATCTCTGATCGTGTTCATGGAGCAGGTTCATCG TGGCATTAAAGGCTTGGTGAGAGATTCACATGGAAAAGGAATCCCAAACGCCATTATCTCCGTAGAAGGCATTAA CCATGACATCCGAACAGCCAACGATGGGGATTACTGGCGCCTCCTGAACCCTGGAGAGTATGTGGTCACAGCAAA GGCCGAAGGTTTCACTGCATCCACCAAGAACTGTATGGTTGGCTATGACATGGGGGGCCACAAGGTGTGACTTCAC ACTTAGCAAAACCAACATGGCCAGGATCCGAGAGATCATGGAGAAGTTTGGGAAGCAGCCCGTCAGCCTGCCAGC CAGGCGGCTGAAGCTGCGGGGGGGGAAGAGACGACAGCGTGGGTGACCCTCCTGGGCCCTTGAGACTCGTCTGGG ${\tt AAGTGCCTGGAAGAGGGTGCATTGTGAGGCAGGTCCCAAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTT}$ CTTTGTTCCCATTTATCCAAATAACTTGGACAGAGCAGCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAG CCAACCTGGGAATCAGAGAGAAGGAGGAGGGGGGGCCTGTCCGTTCAGAGCCTCTGGCTGCATAGAAAAGG ATTCTGGTGCTTCCCCTGTTTGCGTGGCAGCAAGGGTTCCACGTGCATTTGCAATTTGCACAGCTAAAATTGCAG CATTTCCCCAGCTGGCTGTCCCAAATGTTACCATTTGAGATGCTCCCAGGCGTCCTAAGAGAATCCACCTCTC TGGCCCTGGGACATTGCAAGCTGCTACAAATAAATTCTGTGTTCTTTTGACAATAGCGTCATTGCCAAGTGCACA GATCATTCAGGAGTTTGTTGGGCAGCAAGCATGGAGCTTCTTGCACAAATTCTGGGTCCATAAACAACCCCCAAA GTCCCTGCTGATCCAGTAGCCCTGGAGGTTCCCCAGGTAGGGAGAGCCAGAGGTGCCAGCCTTCCTGAAGGGCCA GAAAATTTAGCCTGGATCTCCTCTTTTACCTGCTAGGACTGGAAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTC TCTCTGCTTGAGGTATTGCCCCTGTGTGGAATTGAGTGCTCATGGGTTGGCCTCATATCAGCCTGGGAGTTATTT TTGATATGTAGAATGCCAGATCTTCCAGATTAGGCTAAATGTAATGAAAACCTCTTAGGATTATCTGTGGAGCAT CAGTTTGGGAAGAATTATTGAATTATCTTGCAAGAAAAAGTATGTCTCACTTTTTGTTAATGTTGCTGCCTCAT ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

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FIGURE 392

MSRPGTATPALALVLLAVTLAGVGAQGAALEDPDYYGQEIWSREPYYARPEPELETFSPPLPA
GPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHSVR
VAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCAGRN
DLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIFEGNS
EKEIPVLNELPVPMVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTTTDDLD
FKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEFHYIAGA
HGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNPDGYEKAYEGGSELGGWS
LGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAAETRAVIAW
MEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSYASTHRLMTDARR
RVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHESQLPEEWENNR
ESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRLLNPGEYVVTAKA
EGFTASTKNCMVGYDMGATRCDFTLSKTNMARIREIMEKFGKQPVSLPARRLKLRGRKRRQRG

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FIGURE 393

GTCCCACATCCTGCTCAACTGGGTCAGGTCCCTCTTAGACCAGCTCTTGTCCATCATTTGCTGAAGTGGACCAAC TAGTTCCCCAGTAGGGGGTCTCCCCTGGCAATTCTTGATCGGCGTTTTGGACATCTCAGATCGCTTCCAATGAAGA TGGCCTTGCCTTGCTGCTTGTTTCATAATCATCTAACTATGGGACAAGGTTGTGCCGGCAGCTCTGGGGG AAGGAGCACGGGGCTGATCAAGCCATCCAGGAAACACTGGAGGACTTGTCCAGCCTTGAAAGAACTCTAGTGGTT CTACTTATTTCTTTTAGGGGATTGTCAGGAGGTGACCACTCTCACGGTGAAATACCAAGTGTCAGAGGAAGTGCC ATCTGGTACAGTGATCGGGAAGCTGTCCCAGGAACTGGGCCGGGAGGAGAGGCGGAGGCAAGCTGGGGCCGCCTT GGCTCTGATCCATGTGGAGATCCAAGTGCTGGACATCAATGACCACCAGCCACGGTTTCCCAAAGGCGAGCAGGA GCTGGAAATCTCTGAGAGCGCCTCTCTGCGAACCCGGATCCCCCTGGACAGAGCTCTTGACCCAGACACAGGCCC TAACACCCTGCACACCTCTGTCTCCCAGTGAGCACTTTGCCTTGGATGTCATTGTGGGCCCTGATGAGAC CTATGACAATGGGAACCCCCCAAGTCAGGTACCAGCTTGGTCAAGGTCAACGTCTTGGACTCCAATGACAATAG CCCTGCGTTTGCTGAGAGTTCACTGGCACTGGAAATCCAAGAAGATGCTGCACCTGGTACGCTTCTCATAAAACT GACCGCCACAGACCCTGACCAAGGCCCCAATGGGGAGGTGGAGTTCTTCCTCAGTAAGCACATGCCTCCAGAGGT GCTGGACACCTTCAGTATTGATGCCAAGACAGGCCAGGTCATTCTGCGTCGACCTCTAGACTATGAAAAGAACCC TGCCTACGAGGTGGATGTTCAGGCAAGGGACCTGGGTCCCAATCCTATCCCAGCCCATTGCAAAGTTCTCATCAA GGTTCTGGATGTCAATGACAACATCCCAAGCATCCACGTCACATGGGCCTCCCAGCCATCACTGGTGTCAGAAGC TCTTCCCAAGGACAGTTTTATTGCTCTTGTCATGGCAGATGACTTGGATTCAGGACACAATGGTTTGGTCCACTG CACACTGGACAGAGAGCAGTGGCCCAAATATACCCTCACTCTGTTAGCCCAAGACCAAGGACTCCAGCCCTTATC AGCCAAGAAACAGCTCAGCATTCAGATCAGTGACATCAACGACAATGCACCTGTGTTTGAGAAAAGCAGGTATGA AGTCTCCACGCGGGAAAACAACTTACCCTCTTCACCTCATTACCATCAAGGCTCATGATGCAGACTTGGGCAT TAATGGAAAAGTCTCATACCGCATCCAGGACTCCCCAGTTGCTCACTTAGTAGCTATTGACTCCAACACAGGAGA GGTCACTGCTCAGAGGTCACTGAACTATGAAGAGATGGCCGGCTTTGAGTTCCAGGTGATCGCAGAGGACAGCGG GCAACCCATGCTTGCATCCAGTGTCTCTGTGTGGGTCAGCCTCTTGGATGCCAATGATAATGCCCCAGAGGTGGT CCAGCCTGTGCTCAGCGATGGAAAAGCCAGCCTCTCCGTGCTTGTGAATGCCTCCACAGGCCACCTGCTGGTGCC CATCGAGACTCCCAATGGCTTGGGCCCAGCGGGCACTGACACCTCCACTGGCCACTCACAGCTCCCGGCCATT CCTTTTGACAACCATTGTGGCAAGAGATGCAGACTCGGGGGGCAAATGGAGAGCCCCTCTACAGCATCCGCAATGG CATTGGGAGTGAGTGGGAGCTGGAGATAGTAGTAGAGGACCAGGGAAGCCCCCCTTACAGACCCGAGCCCTGTT GAGGGTCATGTTTGTCACCAGTGTGGACCACCTGAGGGACTCAGCCCGCAAGCCTGGGGCCTTGAGCATGTCGAT GCTGACGGTGATCTGCCTGGCTGTACTGTTGGGCATCTTCGGGTTGATCCTGGCTTTGTTCATGTCCATCTGCCG GACAGAAAAGAAGGACAACAGGGCCTACAACTGTCGGGAGGCCGAGTCCACCTACCGCCAGCAGCCCAAGAGGCC CCACCTCACCCGACCCTGTACAGGACGCTGCGTAATCAAGGCAACCAGGGAGCACCGGCGGAGAGCCGAGAGGT GCTGCAAGACACGGTCAACCTCCTTTTCAACCATCCCAGGCAGAGGAATGCCTCCCGGGAGAACCTGAACCTTCC TGGAGACCAGGGCAGTGAGGAAGCCCCACAGAGGCCACCAGCCTCCTCTGCAACCCTGAGACGGCAGCGACATCT TGCCTTCGCCGAGCGGAACCCCGTGGAGGAGCTCACTGTGGATTCTCCTCCTGTTCAGCAAATCTCCCAGCTGCT AGGGCCTTTGGATCCTGAAGAGGACCTCTCTGTGAAGCAACTGCTAGAAGAAGAGACTGTCAAGTCTGCTGGACCC CACCAACTACCGTGACAATGTGATCTCCCCGGATGCTGCAGCCACGGAGGAGCCGAGGACCTTCCAGACGTTCGG CAAGGCAGAGCCAGAGCTGAGCCCAACAGGCACGAGGCTGGCCAGCACCTTTGTCTCGGAGATGAGCTCACT GCTGGAGATGCTGCTGGAACAGCGCTCCAGCATGCCCGTGGAGGCCGCCTCCGAGGCGCTGCGGCGGCTCTCGGT CTGCGGGAGGACCCTCAGTTTAGACTTGGCCACCAGTGCAGCCTCAGGCATGAAAGTGCAAGGGGACCCAGGTGG AAAGACGGGGACTGAGGGCAAGAGCAGAGCAGCAGCAGCAGCAGGTGCCTG<u>TGA</u>ACATACCTCAGACGCCT CGGCGGCCTGAGAACTTTAGGGTGACTGATGCTACCCCCACAGAGGGGGGCAAGAGCCCCAGGACTAACAGCTGAC TGACCAAAGCAGCCCCTTGTAAGCAGCTCTGAGTCTTTTGGAGGACAGGGACGGTTTGTGGCTGAGATAAGTGTT AAAGGGTGGCCTTCTTGGGTAGCAGGAGTCAGGGGGCTGTACCCTGGGGGTGCCAGGAAATGCTCTCTGACCTAT CAATAAAGGAAAAGCAGTAAAAAAAAAAAAAAAAAAA

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FIGURE 394

MMQLLQLLLGLLGPGGYLFLLGDCQEVTTLTVKYQVSEEVPSGTVIGKLSQELGREERRRQAG AAFQVLQLPQALPIQVDSEEGLLSTGRRLDREQLCRQWDPCLVSFDVLATGDLALIHVEIQVL DINDHOPRFPKGEOELEISESASLRTRIPLDRALDPDTGPNTLHTYTLSPSEHFALDVIVGPD ETKHAELIVVKELDREIHSFFDLVLTAYDNGNPPKSGTSLVKVNVLDSNDNSPAFAESSLALE IQEDAAPGTLLIKLTATDPDOGPNGEVEFFLSKHMPPEVLDTFSIDAKTGQVILRRPLDYEKN PAYEVDVQARDLGPNPIPAHCKVLIKVLDVNDNIPSIHVTWASQPSLVSEALPKDSFIALVMA DDLDSGHNGLVHCWLSQELGHFRLKRTNGNTYMLLTNATLDREQWPKYTLTLLAQDQGLQPLS AKKQLSIQISDINDNAPVFEKSRYEVSTRENNLPSLHLITIKAHDADLGINGKVSYRIQDSPV AHLVAIDSNTGEVTAQRSLNYEEMAGFEFQVIAEDSGQPMLASSVSVWVSLLDANDNAPEVVQ PVLSDGKASLSVLVNASTGHLLVPIETPNGLGPAGTDTPPLATHSSRPFLLTTIVARDADSGA NGEPLYSIRNGNEAHLFILNPHTGOLFVNVTNASSLIGSEWELEIVVEDOGSPPLOTRALLRV MFVTSVDHLRDSARKPGALSMSMLTVICLAVLLGIFGLILALFMSICRTEKKDNRAYNCREAE STYRQQPKRPQKHIQKADIHLVPVLRGQAGEPCEVGQSHKDVDKEAMMEAGWDPCLQAPFHLT PTLYRTLRNQGNQGAPAESREVLQDTVNLLFNHPRQRNASRENLNLPEPQPATGQPRSRPLKV AGSPTGRLAGDQGSEEAPORPPASSATLRRORHLNGKVSPEKESGPRQILRSLVRLSVAAFAE RNPVEELTVDSPPVOOISOLLSLLHOGOFOPKPNHRGNKYLAKPGGSRSAIPDTDGPSARAGG QTDPEQEEGPLDPEEDLSVKQLLEEELSSLLDPSTGLALDRLSAPDPAWMARLSLPLTTNYRD NVISPDAAATEEPRTFQTFGKAEAPELSPTGTRLASTFVSEMSSLLEMLLEQRSSMPVEAASE ALRRLSVCGRTLSLDLATSAASGMKVQGDPGGKTGTEGKSRGSSSSSRCL

Important features:

Signal peptide:

amino acids 1-13

Transmembrane domain:

amino acids 719-739

N-glycosylation site.

amino acids 415-418, 582-585, 659-662, 662-665 amd 857-860

Cadherins extracellular repeated domain signature.

amino acids 123-133, 232-242, 340-350, 448-458 and 553-563

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FIGURE 395

CCCAGGCTCTAGTGCAGGAGGAGGAGGAGGAGGAGGAGGTGGAGATTCCCAGTTAAAAGG CTCCAGAATCGTGTACCAGGCAGAGAACTGAAGTACTGGGGCCTCCTCCACTGGGTCCGAATC AGTAGGTGACCCCGCCCTGGATTCTGGAAGACCTCACCATGGGACGCCCCCGACCTCGTGCG GCCAAGACGTGGATGTTCCTGCTCTTGCTGGGGGGAGCCTGGGCAGGACACTCCAGGGCACAG GAGGACAAGGTGCTGGGGGGTCATGAGTGCCAACCCCATTCGCAGCCTTGGCAGGCGGCCTTG TTCCAGGGCCAGCAACTACTCTGTGGCGGTGTCCTTGTAGGTGGCAACTGGGTCCTTACAGCT GCCCACTGTAAAAAACCGAAATACACAGTACGCCTGGGAGACCACAGCCTACAGAATAAAGAT GGCCCAGAGCAAGAAATACCTGTGGTTCAGTCCATCCCACACCCCTGCTACAACAGCAGCGAT GTGGAGGACCACAACCATGATCTGATGCTTCTTCAACTGCGTGACCAGGCATCCCTGGGGTCC AAAGTGAAGCCCATCAGCCTGGCAGATCATTGCACCCAGCCTGGCCAGAAGTGCACCGTCTCA GGCTGGGGCACTGTCACCAGTCCCCGAGAGAATTTTCCTGACACTCTCAACTGTGCAGAAGTA AAAATCTTTCCCCAGAAGAAGTGTGAGGATGCTTACCCGGGGCAGATCACAGATGGCATGGTC TGTGCAGGCAGCAAAGGGGCTGACACGTGCCAGGGCGATTCTGGAGGCCCCCTGGTGTGT GATGGTGCACTCCAGGGCATCACATCCTGGGGGCTCAGACCCCTGTGGGAGGTCCGACAAACCT GGCGTCTATACCAACATCTGCCGCTACCTGGACTGGATCAAGAAGATCATAGGCAGCAAGGGC **TGA**TTCTAGGATAAGCACTAGATCTCCCTTAATAAACTCACAACTCTCTGGTTC

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FIGURE 396

MGRPRPRAAKTWMFLLLLGGAWAGHSRAQEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLV GGNWVLTAAHCKKPKYTVRLGDHSLQNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQL RDQASLGSKVKPISLADHCTQPGQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYP GQITDGMVCAGSSKGADTCQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWI KKIIGSKG

Important Features:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 51-71

N-glycosylation site.

amino acids 110-113

Serine proteases, trypsin family, histidine active site.

amino acids 69-74 and 207-217

Tyrosine kinase phosphorylation site.

amino acids 182-188

Kringle domain proteins motif

amino acids 205-217

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FIGURE 397

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGGATCCAGAGCC**ATG**TCGGACCTGCTAC TACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTGCCGGGT ACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTCACCCCCCATCCGCAACGTCACTG TGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGCTGCA GCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCCCCCTG ATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCCCTGAGC TCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGCCATGTGG CTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGGAGATCTACC AGGAAGACCAGATCCATTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTATGTGCCTGAGA TGAAGGAGACAGAGTGGAAATGGCGGGGGCTTGTGGAGGCCATTGACACCCAGGTGGATGGCA CAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCCCTGGCAGCCGGG AGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCAGCCGTGGCTGGGATGACGGTGACACCC GCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGAGGAGCTGGACTTGG AGGGCGAGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGCCCCTGGGGACTACCA AGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAGTAACCCATGGCCTGCACCCTCC TGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCTCCAGCCCTCTTCCTCCT TCCTCTGGGGGAGGAGGGGTTCCTGAGGGACCTGACTTCCCCTGCTCCAGGCCTCTTGCTAAG CCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCAGGGACTATTTTCTGCACCA GCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTCAGACTCACAGTGGAGCTTCCAGGACC

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FIGURE 398

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGLYGETGRL FTESCSISPKLRSIAVYYDNPHMVPPDKCRCAVGSILSEGEESPSPELIDLYQKFGFKVFSFP APSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPLARQGD FYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAATLSPGASSRGW DDGDTRSEHSYSESGASGSSFEELDLEGEGPLGESRLDPGTEPLGTTKWLWEPTAPEKGKE

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FIGURE 399

GGACGAGGCAGATCTCGTTCTGGGGCAAGCCGTTGACACTCGCTCCCTGCCACCGCCCGGGC TCCGTGCCGCCAAGTTTTCATTTTCCACCTTCTCTGCCTCCAGTCCCCCAGCCCCTGGCCGAG AGAAGGGTCTTACCGGCCGGGATTGCTGGAAACACCAAGAGGTGGTTTTTGTTTTTTAAAACT TCTGTTTCTTGGGAGGGGTGTGGCGGGGCAGGATGAGCAACTCCGTTCCTCTGTTTTC TGGAGCCTCTGCTATTGCTTTGCTGCGGGGAGCCCCGTACCTTTTGGTCCAGAGGGACGGCTG GAAGATAAGCTCCACAAACCCAAAGCTACACAGACTGAGGTCAAACCATCTGTGAGGTTTAAC TTAGAAGACTGCAGTTTCAACATGACAGCTAAAACCTTTTTCATCATTCACGGATGGACGATG AGCGGTATCTTTGAAAACTGGCTGCACAAACTCGTGTCAGCCCTGCACACAAGAGAGAAAAGAC GCCAATGTAGTTGTGGTTGACTGGCTCCCCTGGCCCACCAGCTTTACACGGATGCGGTCAAT AATACCAGGGTGGTGGGACACAGCATTGCCAGGATGCTCGACTGGCTGCAGGAGAAGGACGAT TTTTCTCTCGGGAATGTCCACTTGATCGGCTACAGCCTCGGAGCGCACGTGGCCGGGTATGCA GGCAACTTCGTGAAAGGAACGGTGGGCCGAATCACAGGTTTGGATCCTGCCGGGCCCATGTTT GAAGGGCCGACATCCACAAGAGGCTCTCTCCGGACGATGCAGATTTTGTGGATGTCCTCCAC ACCTACACGCGTTCCTTCGGCTTGAGCATTGGTATTCAGATGCCTGTGGGCCACATTGACATC TACCCCAATGGGGGTGACTTCCAGCCAGGCTGTGGACTCAACGATGTCTTGGGATCAATTGCA TCTCTGGTGAATCAGGACAAGCCGAGTTTTGCCTTCCAGTGCACTGACTCCAATCGCTTCAAA AAGGGGATCTGTCTGAGCTGCCGCAAGAACCGTTGTAATAGCATTGGCTACAATGCCAAGAAA AACCTTCAGTCCCTGGAGTGTCCCTGAGGAAGGCCCTTAATACCTCCTTCTTAATACCATGCT GCAGAGCAGGGCACATCCTAGCCCAGGAGAAGTGGCCAGCAATCCAATCAAATCGTTGCAA ATCAGATTACACTGTGCATGTCCTAGGAAAGGGAATCTTTACAAAATAAACAGTGTGGACCCC

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FIGURE 400

MSNSVPLLCFWSLCYCFAAGSPVPFGPEGRLEDKLHKPKATQTEVKPSVRFNLRTSKDPEHEG
CYLSVGHSQPLEDCSFNMTAKTFFIIHGWTMSGIFENWLHKLVSALHTREKDANVVVVDWLPL
AHQLYTDAVNNTRVVGHSIARMLDWLQEKDDFSLGNVHLIGYSLGAHVAGYAGNFVKGTVGRI
TGLDPAGPMFEGADIHKRLSPDDADFVDVLHTYTRSFGLSIGIQMPVGHIDIYPNGGDFQPGC
GLNDVLGSIAYGTITEVVKCEHERAVHLFVDSLVNQDKPSFAFQCTDSNRFKKGICLSCRKNR
CNSIGYNAKKMRNKRNSKMYLKTRAGMPFRGNLQSLECP

Important features:

Signal peptide:

amino acids 1-16

Lipases, serine active site.

amino acids 163-172

N-glycosylation sites.

amino acids 80-83 and 136-139

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FIGURE 401

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FIGURE 402

 ${\tt MACRCLSFLLMGTFLSVSQTVLAQLDALLVFPGQVAQLSCTLSPQHVTIRDYGVSWYQQRAGS}$ ${\tt APRYLLYYRSEEDHHRPADIPDRFSAAKDEAHNACVLTISPVQPEDDADYYCSVGYGFSP}$

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FIGURE 403

GCAGAGCAGGGCTGCATTTCCAGCAGGAGCTGCGAGCACAGTGCTGGCTCACAACAACAAGATGCTCAAGGTGTCAGC CGTACTGTGTGTGTGCAGCCGCTTGGTGCAGTCAGTCTCTCGCAGCTGCCGCGGCGGTGGCTGCAGCCGGGGG GCGGTCGGACGCCGTAATTTTCTGGATGATAAACAATGGCTCACCACAATCTCTCAGTATGACAAGGAAGTCGG ACAGTGGAACAAATTCCGAGACGAAGTAGAGGATGATTATTTCCGCACTTGGAGTCCAGGAAAACCCTTCGATCA GGCTTTAGATCCAGCTAAGGATCCATGCTTAAAGATGAAATGTAGTCGCCATAAAGTATGCATTGCTCAAGATTC TCAGACTGCAGTCTGCATTAGTCACCGGAGGCTTACACACAGGATGAAAGAAGCAGGAGTAGACCATAGGCAGTG GAGGGGTCCCATATTATCCACCTGCAAGCAGTGCCCAGTGGTCTATCCCAGCCCTGTTTGTGGTTCAGATGGTCA TACCTACTCTTTTCAGTGCAAACTAGAATATCAGGCATGTGTCTTAGGAAAACAGATCTCAGTCAAATGTGAAGG ACATTGCCCATGTCCTTCAGATAAGCCCACCAGTACAAGCAGAAATGTTAAGAGAGCATGCAGTGACCTGGAGTT CAGGGAAGTGGCAAACAGATTGCGGGACTGGTTCAAGGCCCTTCATGAAAGTGGAAGTCAAAACAAGAAGACAAA AACATTGCTGAGGCCTGAGAGAAGCAGATTCGATACCAGCATCTTGCCAATTTGCAAGGACTCACTTGGCTGGAT GTTTAACAGACTTGATACAAACTATGACCTGCTATTGGACCAGTCAGAGCTCAGAAGCATTTACCTTGATAAGAA TGAACAGTGTACCAAGGCATTCTTCAATTCTTGTGACACATACAAGGACAGTTTAATATCTAATAATGAGTGGTG CTACTGCTTCCAGAGACAGCAAGACCCACCTTGCCAGACTGAGCTCAGCAATATTCAGAAGCGGCAAGGGGTAAA GAAGCTCCTAGGACAGTATATCCCCCTGTGTGATGAAGATGGTTACTACAAGCCAACACAATGTCATGGCAGTGT TGGACAGTGCTGGTGTTGACAGATATGGAAATGAAGTCATGGGATCCAGAATAAATGGTGTTGCAGATTGTGC TATAGATTTTGAGATCTCCGGAGATTTTGCTAGTGGCGATTTTCATGAATGGACTGATGATGAGGATGATGAAGA CCATGATGTATACATT<u>TGA</u>TTGATGACAGTTGAAATCAATAAATTCTACATTTCTAATATTTTACAAAAATGATAG CCTATTTAAAATTATCTTCTCCCCAATAACAAAATGATTCTAAACCTCACATATATTTTGTATAATTATTTGAA AAATTGCAGCTAAAGTTATAGAACTTTATGTTTAAATAAGAATCATTTGCTTTGAGTTTTTATATTCCTTACACA AAAAGAAAATACATATGCAGTCTAGTCAGACAAAATAAAGTTTTGAAGTGCTACTATAATAAATTTTTCACGAGA ACAAACTTTGTAAATCTTCCATAAGCAAAATGACAGCTAGTGCTTGGGATCGTACATGTTAATTTTTTGAAAGAT TTAATTGCATTTCCAAAGTAGCATCTTGCTAGACCTAGATGAGTCAGGATAACAGAGAGATACCACATGACTCCA ΑΑΑΑΑΑΑΑΑΑΑ

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FIGURE 404

MLKVSAVLCVCAAAWCSQSLAAAAAVAAAGGRSDGGNFLDDKQWLTTISQYDKEVGQWNKFRD EVEDDYFRTWSPGKPFDQALDPAKDPCLKMKCSRHKVCIAQDSQTAVCISHRRLTHRMKEAGV DHRQWRGPILSTCKQCPVVYPSPVCGSDGHTYSFQCKLEYQACVLGKQISVKCEGHCPCPSDK PTSTSRNVKRACSDLEFREVANRLRDWFKALHESGSQNKKTKTLLRPERSRFDTSILPICKDS LGWMFNRLDTNYDLLLDQSELRSIYLDKNEQCTKAFFNSCDTYKDSLISNNEWCYCFQRQQDP PCQTELSNIQKRQGVKKLLGQYIPLCDEDGYYKPTQCHGSVGQCWCVDRYGNEVMGSRINGVA DCAIDFEISGDFASGDFHEWTDDEDDEDDIMNDEDEIEDDDEDGGDDDDGGDDHDVYI

Important features:

Signal peptide:

amino acids 1-16

Leucine zipper pattern.

amino acids 246-267

N-myristoylation sites.

amino acids 357-362, 371-376 and 376-381

Thyroglobulin type-1 repeat proteins

amino acids 353-365 and 339-352

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FIGURE 405

GGAAGGGGAGGAGCACACACAGGCACAGGCCGTGAGGGACCTGCCCAGACCTGGAGGGTCTCGCTCTGTCA CACAGGCTGGAGTGCAGTGGTGATCTTGGCTCATCGTAACCTCCACCTCCCGGGTTCAAGTGATTCTCATGCC ${\tt TCAGCCTCCCGAGTAGCTGGGATTACAGGTGGTGACTTCCAAGAGTGACTCCGTCGGAGGAAA \\ \underline{{\tt ATG}} {\tt ACTCCCCAG} \\$ GAAGACTTTCGCTTCTGCAGCCAGCGGAACCAGACACACAGGAGCAGCCTCCACTACAAACCCACACCAGACCTG CGCATCTCCATCGAGAACTCCGAAGAGGCCCTCACAGTCCATGCCCCTTTCCCTGCAGCCCACCCTGCTTCCCGA TCCTTCCCTGACCCCAGGGGCCTCTACCACTTCTGCCTCTACTGGAACCGACATGCTGGGAGATTACATCTTCTC TATGGCAAGCGTGACTTCTTGCTGAGTGACAAAGCCTCTAGCCTCCTCTGCTTCCAGCACCAGGAGGAGAGCCTG GCTCAGGGCCCCCGCTGTTAGCCACTTCTGTCACCTCCTGGTGGAGCCCTCAGAACATCAGCCTGCCCAGTGCC GCCAGCTTCACCTTCCCCCACAGTCCTCCCCACACGCCGCTCACAATGCCTCGGTGGACATGTGCGAGCTC AAAAGGACCTCCAGCTGCTCAGCCAGTTCCTGAAGCATCCCCAGAAGGCCTCAAGGAGGCCCTCGGCTGCCCCC GCCAGCCAGCAGTTGCAGAGCCTGGAGTCGAAACTGACCTCTGTGAGATTCATGGGGGACATGGTGTCCTTCGAG GAGGACCGGATCAACGCCACGGTGTGGAAGCTCCAGCCCACAGCCGGCCTCCAGGACCTGCACATCCACTCCCGG CAGGAGGAGGAGCAGAGCGAGATCATGGAGTACTCGGTGCTGCCTCGAACACTCTTCCAGAGGACGAAAAGGC CGGAGCGGGGAGGCTGAGAAGAGACTCCTCCTGGTGGACTTCAGCAGCCAAGCCCTGTTCCAGGACAAGAATTCC AGCCAAGTCCTGGGTGAGAAGGTCTTGGGGATTGTGGTACAGAACACCAAAGTAGCCAACCTCACGGAGCCCGTG GTGCTCACTTTCCAGCACCAGCTACAGCCGAAGAATGTGACTCTGCAATGTGTGTTCTGGGTTGAAGACCCCACA TTGAGCAGCCCGGGGCATTGGAGCAGTGCTGGGTGTGAGACCGTCAGGAGAAAACCCAAACATCCTGCTTCTGC AACCACTTGACCTACTTTGCAGTGCTGATGGTCTCCTCGGTGGAGGTGGACGCCGTGCACAAGCACTACCTGAGC GTGCCCCTGCCGTGCAGGAGGAAACCTCGGGACTACACCATCAAGGTGCACATGAACCTGCTGCTGGCCGTCTTC ATCTTCCTGCACTTCTCCCTGCTCACCTGCCTTTCCTGGATGGGCCTCGAGGGGTACAACCTCTACCGACTCGTG GTGGAGGTCTTTGGCACCTATGTCCCTGGCTACCTACTCAAGCTGAGCGCCATGGGCTGGGGCTTCCCCATCTTT $\tt CTGGTGACGCTGGTGGCTGGATGTGGACAACTATGGCCCCATCATCTTGGCTGTGCATAGGACTCCAGAG$ GGCGTCATCTACCCTTCCATGTGCTGGATCCGGGACTCCCTGGTCAGCTACATCACCAACCTGGGCCTCTTCAGC CTGGTGTTCTGTTCAACATGGCCATGCTAGCCACCATGGTGGTGCAGATCCTGCGGCTGCGCCCCCACACCCAA AAGTGGTCACATGTGCTGACACTGCTGGGCCTCAGCCTGGTCCTTGGCCTGCCCTGGGCCTTGATCTTCTTCTCCC TTTGCTTCTGGCACCTTCCAGCTTGTCGTCCTCTACCTTTTCAGCATCATCACCTCCTTCCAAGGCTTCCTCATC TTCATCTGGTACTGGTCCATGCGGCTGCAGGCCCGGGGTGGCCCCTCCCCTCTGAAGAGCAACTCAGACAGCGCC AGGCTCCCCATCAGCTCGGCCACCTCGTCCAGCCGCATCTAGGCCTCCAGCCCACCTGCCCATGTGATGAAG ${\tt GCCTTGGGGACTACTCGGCTCTCACTCAGCTCCCACGGGACTCAGAAGTGCGCCGCCATGCTGCCTAGGGTACTG}$ TCCCCACATCTGTCCCAACCCAGCTGGAGGCCTGGTCTCTTCCTTACAACCCCTGGGCCCAGCCCTCATTGCTGGG GTTGCTCTGTCTCGTGGTCACCCTGAGGGCACTCTGCATCCTCTGTCATTTTAACCTCAGGTGGCACCCAGGG CGAATGGGGCCCAGGGCAGACCTTCAGGGCCAGAGCCCTGGCGGAGAGAGGCCCTTTGCCAGGAGCACAGCAGC TCCTCCTCCCAGGGCCTCCTTGCTCCTTCGTTCACAGCTGGGGGTCCCCGATTCCAATGCTGTTTTTTTGGGGA GTGGTTTCCAGGAGCTGCCTGGTGTCTGCTGTAAATGTTTGTCTACTGCACAAGCCTCGGCCTGCCCCTGAGCCA GGCTCGGTACCGATGCGTGGGCTGGGCTAGGTCCCTCTGTCCATCTGGGCCTTTGTATGAGCTGCATTGCCCTTG CTCACCCTGACCAAGCACACGCCTCAGAGGGGCCCTCAGCCTCTCCTGAAGCCCTCTTGTGGCAAGAACTGTGGA CCATGCCAGTCCGTCTGGTTTCCATCCACCACTCCAAGGACTGAGACTGACCTCCTCTGGTGACACTGGCCTA GAGCCTGACACTCTCCTAAGAGGTTCTCTCCAAGCCCCCAAATAGCTCCAGGCGCCCTCGGCCCCCATCATGGT GGGAGCCATCATTCCTGCCTGGGAATCCTGGAAGACTTCCTGCAGGAGTCAGCGTTCAATCTTGACCTTGAAGAT GGGAAGGATGTTCTTTTACGTACCAATTCTTTTGTCTTTTGATATTAAAAAAGAAGTACATGTTCATTGTAGAGA

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FIGURE 406

MTPQSLLQTTLFLLSLLFLVQGAHGRGHREDFRFCSQRNQTHRSSLHYKPTPDLRISIENSEE
ALTVHAPFPAAHPASRSFPDPRGLYHFCLYWNRHAGRLHLLYGKRDFLLSDKASSLLCFQHQE
ESLAQGPPLLATSVTSWWSPQNISLPSAASFTFSFHSPPHTAAHNASVDMCELKRDLQLLSQF
LKHPQKASRRPSAAPASQQLQSLESKLTSVRFMGDMVSFEEDRINATVWKLQPTAGLQDLHIH
SRQEEEQSEIMEYSVLLPRTLFQRTKGRSGEAEKRLLLVDFSSQALFQDKNSSQVLGEKVLGI
VVQNTKVANLTEPVVLTFQHQLQPKNVTLQCVFWVEDPTLSSPGHWSSAGCETVRRETQTSCF
CNHLTYFAVLMVSSVEVDAVHKHYLSLLSYVGCVVSALACLVTIAAYLCSRVPLPCRRKPRDY
TIKVHMNLLLAVFLLDTSFLLSEPVALTGSEAGCRASAIFLHFSLLTCLSWMGLEGYNLYRLV
VEVFGTYVPGYLLKLSAMGWGFPIFLVTLVALVDVDNYGPIILAVHRTPEGVIYPSMCWIRDS
LVSYITNLGLFSLVFLFNMAMLATMVVQILRLRPHTQKWSHVLTLLGLSLVLGLPWALIFFSF
ASGTFQLVVLYLFSIITSFQGFLIFIWYWSMRLQARGGPSPLKSNSDSARLPISSGSTSSSRI

Important features:

Signal peptide:

amino acids 1-25

Putative transmembrane domains:

amino acids 382-398, 402-420, 445-468, 473-491, 519-537, 568-590 and 634-657

Microbodies C-terminal targeting signal.

amino acids 691-693

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 198-201 and 370-373

N-glycosylation sites.

amino acids 39-42, 148-151, 171-174, 234-237, 303-306, 324-327 and 341-344

G-protein coupled receptors family 2 proteins

amino acids 475-504

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FIGURE 407

TTGTGACTAAAAGCTGGCCTAGCAGGCCAGGGAGTGCAGCTGCAGGCGTGGGGGTGGCAGGAG CCGCAGAGCCAGACCAGCCGAGAAACAGGTGGACAGTGTGAAAGAACCAGTGGTCTCGC TCTGTTGCCCAGGCTAGAGTGTACTGGCGTGATCATAGCTCACTGCAGCCTCAGACTCCTGGA CTTGAGAAATCCTCCTGCCTTAGCCTCCTGCATATCTGGGACTCCAGGGGTGCACTCAAGCCC TGTTTCTTCTCTGTGAGTGGACCACGGAGGCTGGTGAGCTGCCTGTCATCCCAAAGCTC AGCTCTGAGCCAGAGTGGTGGTGGCTCCACCTCTGCCGCCGGCATAGAAGCCAGGAGCAGGGC TCTCAGAAGGCGGTGGTGCCCAGCTGGGATC**ATG**TTGTTGGCCCTGGTCTGTCTGCTCAGCTG CCTGCTACCCTCCAGTGAGGCCAAGCTCTACGGTCGTTGTGAACTGGCCAGAGTGCTACATGA CTTCGGGCTGACGGATACCGGGGATACAGCCTGGCTGACTGGGTCTGCCTTGCTTATTTCAC AAGCGGTTTCAACGCAGCTGCTTTGGACTACGAGGCTGATGGGAGCACCAACAACGGGATCTT CCAGATCAACAGCCGGAGGTGGTGCAGCAACCTCACCCCGAACGTCCCCAACGTGTGCCGGAT GTACTGCTCAGATTTGTTGAATCCTAATCTCAAGGATACCGTTATCTGTGCCATGAAGATAAC CCAAGAGCCTCAGGGTCTGGGTTACTGGGAGGCCTGGAGGCATCACTGCCAGGGAAAAGACCT CACTGAATGGGTGGATGGCTGTGACTTC**TAG**GATGGACGGAACCATGCACAGCAGGCTGGGAA ATGTGGTTTGGTTCCTGACCTAGGCTTGGGAAGACAAGCCAGCGAATAAAGGATGGTTGAACG **TGAAA**

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FIGURE 408

MLLALVCLLSCLLPSSEAKLYGRCELARVLHDFGLDGYRGYSLADWVCLAYFTSGFNAAALDY EADGSTNNGIFQINSRRWCSNLTPNVPNVCRMYCSDLLNPNLKDTVICAMKITQEPQGLGYWE AWRHHCQGKDLTEWVDGCDF

Important features:

Signal peptide:

amino acids 1-18

N-myristoylation site.

amino acids 67-72

Homolgous region to Alpha-lactalbumin / lysozyme C proteins. amino acids 34-58 (catalytic domain), 111-132 and 66-107

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FIGURE 409

CAGACTCCAGATTTCCCTGTCAACCACGAGGAGTCCAGAGAGGAAACGCGGAGCGGAGCAACAGTACCTGACGC CTCTTTCAGCCCGGGATCGCCCCAGCAGGGATCGGCGACAAGATCTGGCTGCCCTTCCCCGTGCTCCTTCTGGCC GCTCTGCCTCCGGTGCTGCCTGGGGCCGGCCTCCACACCTTCCCTCGATAGCGACTTCACCTTTACCCTT CCCGCCGGCCAGAAGGAGTGCTTCTACCAGCCCATGCCCCTGAAGGCCTCGCTGGAGATCGAGTACCAAGTTTTA GATGGAGCAGGATTAGATATTGATTTCCATCTTGCCTCTCCAGAAGGCAAAACCTTAGTTTTTGAACAAAGAAAA TCAGATGGAGTTCACACTGTAGAGACTGAAGTTGGTGATTACATGTTCTGCTTTGACAATACATTCAGCACCATT TCTGAGAAGGTGATTTTCTTTGAATTAATCCTGGATAATATGGGAGAACAGGCACAAGAACAAGAAGATTGGAAG AAATATATTACTGGCACAGATATATTGGATATGAAACTGGAAGACATCCTGGAATCCATCAACAGCATCAAGTCC AGACTAAGCAAAAGTGGGCACATACAAATTCTGCTTAGAGCATTTGAAGCTCGTGATCGAAACATACAAGAAAGC **AACTTTGATAGAGTCAATTTCTGGTCTATGGTTAATTTAGTGGTCATGGTGGTGGTGTCAGCCATTCAAGTTTAT** ATGCTGAAGAGTCTGTTTGAAGATAAGAGGAAAAGTAGAACT<u>TAA</u>AACTCCAAACTAGAGTACGTAACATTGAAA AATGAGGCATAAAAATGCAATAAACTGTTACAGTCAAGACCATTAATGGTCTTCTCCAAAATATTTTGAGATATA AAAGTAGGAAACAGGTATAATTTTAATGTGAAAATTAAGTCTTCACTTTCTGTGCAAGTAATCCTGCTGATCCAG AGTCTGTTTTTAACAGGTTCTATTACCCAGAACTTTTTTGTAAATGCGGCAGTTACAAATTAACTGTGGAAGTTT TCAGTTTTAAGTTATAAATCACCTGAGAATTACCTAATGATGGATTGAATAAATCTTTAGACTACAAAAGCCCAA CTTTTCTCTATTTACATATGCATCTCTCCTATAATGTAAATAGAATAATAGCTTTGAAATACAATTAGGTTTTTG AGATTTTTATAACCAAATACATTTCAGTGTAACATATTAGCAGAAAGCATTAGTCTTTGTACTTTGCTTACATTC CCAAAAGCTGACATTTTCACGATTCTTAAAAACACAAAGTTACACTTACTAAAAATTAGGACATGTTTTCTCTTTG AAATGAAGAATATAGTTTAAAAGCTTCCTCCTCCATAGGGACACATTTTCTCTAACCCTTAACTAAAGTGTAGGA TTTTAAAATTAAATGTGAGGTAAAATAAGTTTATTTTAATAGTATCTGTCAAGTTAATATCTGTCAACAGTTAA TAATCATGTTATGTTAACTTTAACATGATTGCTGACTTGGATAATTCATTATCAGCAGCAGTTATGAAGGAAATA TTGCTAAAATGATCTGGGCCTACCATAAATAAATATCTCCTTTTCTGAGCTCTAAGAATTATCAGAAAACAGGAA AAACTTTGGCTGTAGGTTTTTATTTTCTACAAGAATTCTGGTTTGAATTATTTTTGTAAGCAGGTACATTTTATA TAAAATGGCCTTTCTGAACACTTTATTTATTGATGTTGAAGTAAGGATTAGAAACATAGACTCCCAAGTTTTAAA CACCTAAATGTGAATAACCCATATATACAACAAAGTTTCTGCCATCTAGCTTTTTGAAGTCTATGGGGGTCTTAC TCAAGTACTAGTAATTTAACTTCATCATGAATGAACTATAATTTTTAAGTTATGCCCATTTATAACGTTGTTTAT GACTACATTGTGAGTTAGAAACAAACTTAAAATTTGGGGTATAGAACCCCTCAACAGGTTAGTAATGCTGGAATT CTTGATGAGCAATAATGATAACCAGAGAGTGATTTCATTTACACTCATAGTAGTATAAAAAGAGATACATTTCCC TCTTAGGCCCCTGGGAGAAGAGCAGCTTAGATTTCCCTACTGGCAAGGTTTTTAAAAATGAGGTAAATGCCGTAT ATGATCAATTACCTTAATTGGCCAAGAAAATGCTTCAGGTGTCTAGGGGTATCCTCTGCAACACTTGCAGAACAA AGGTCAATAAGATCCTTGCCTATGAATACCCCTCCCTTTTGCGCTGTTAAATTTGCAATGAGAAGCAAATTTACA GTACCATAACTAATAAAGCAGGGTACAGATATAAACTACTGCATCTTTTCTATAAAACTGTGATTAAGAATTCTA CCTCTCCTGTATGGCTGTTACTGTACTGTACTCTCTGACTCCTTACCTAACAATGAATTTGTTACATAATCTTCT ACATGTATGATTTGTGCCACTGATCTTAAACCTATGATTCAGTAACTTCTTACCATATAAAAACGATAATTGCTT TATTTGGAAAAGAATTTAGGAATACTAAGGACAATTATTTTTATAGACAAAGTAAAAAGACAGATATTTAAGAGG CATAACCAAAAAAGCAAAACTTGTAAACAGAGTAAAAATCTTTAATATTTCTAAAGACATACTGTTTATCTGCTT CATATGCTTTTTTTAATTTCACTATTCCATTTCTAAATTAAAGTTATGCTAAATTGAGTAAGCTGTTTATCACTT AACAGCTCATTTTGTCTTTTTCAATATACAAATTTTAAAAATACTACAATATTTAACTAAGGCCCAACCGATTTC CATAATGTAGCAGTTACCGTGTTCACCTCACACTAAGGCCTAGAGTTTGCTCTGATATGCATTTGGATGATTAAT GTTATGCTGTTCTTTCATGTGAATGTCAAGACATGGAGGGTGTTTGTAATTTTATGGTAAAATTAATCCTTCTTA CACATAATGGTGTCTTAAAATTGACAAAAAATGAGCACTTACAATTGTATGTCTCCTCAAATGAAGATTCTTTAT GTGAAATTTTAAAAGACATTGATTCCGCATGTAAGGATTTTTCATCTGAAGTACAATAATGCACAATCAGTGTTG AAATTATCAAAGGAAAA

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FIGURE 410

MGDKIWLPFPVLLLAALPPVLLPGAAGFTPSLDSDFTFTLPAGQKECFYQPMPLKASLEIEYQ VLDGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVETEVGDYMFCFDNTFSTISEKVIFFELIL DNMGEQAQEQEDWKKYITGTDILDMKLEDILESINSIKSRLSKSGHIQILLRAFEARDRNIQE SNFDRVNFWSMVNLVVMVVVSAIQVYMLKSLFEDKRKSRT

Important features:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 195-217

N-myristoylation site.

amino acids 43-48

Tyrosine kinase phosphorylation site.

amino acids 55-62

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FIGURE 411

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAAACTTCCCAGGGGACCGCATTCCAGAGTCA

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FIGURE 412

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESPGEWTTWFNID YPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQRP GQNCSNYTVRFLCPPGSLRRDTERIWSPWSPWSKCSAACGQTGVQTRTRICLAEMVSLCSEAS EEGQHCMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAIYLLTKTPKL LTQTDSDGRFRIPGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPYMVMNP ETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRKLQQHQAGEYFCKA QSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQNATNSFYYDVGRCPVKTCAGQQ DNGIRCRDAVQNCCGISKTEEREIQCSGYTLPTKVAKECSCQRCTETRSIVRGRVSAADNGEP MRFGHVYMGNSRVSMTGYKGTFTLHVPQDTERLVLTFVDRLOKFVNTTKVLPFNKKGSAVFHE IKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSRSFYRQNGEPYIGKVKASVTFLDPR NISTATAAQTDLNFINDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHLDSTQVKMPEHI STVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNLDVPESRRCFVKV RAYRSERFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGACVPAFCDDQSPDA YSAYVLASLAGEELQAVESSPKFNPNAIGVPOPYLNKLNYRRTDHEDPRVKKTAFQISMAKPR PNSAEESNGPIYAFENLRACEEAPPSAAHFRFYOIEGDRYDYNTVPFNEDDPMSWTEDYLAWW PKPMEFRACYIKVKIVGPLEVNVRSRNMGGTHRRTVGKLYGIRDVRSTRDRDOPNVSAACLEF KCSGMLYDQDRVDRTLVKVIPQGSCRRASVNPMLHEYLVNHLPLAVNNDTSEYTMLAPLDPLG HNYGIYTVTDQDPRTAKEIALGRCFDGTSDGSSRIMKSNVGVALTFNCVERQVGRQSAFQYLQ STPAQSPAAGTVQGRVPSRRQQRASRGGQRQGGVVASLRFPRVAQQPLIN

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FIGURE 413

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FIGURE 414

 ${\tt MGPSSCLLLILIPLLQLINPGSTQCSLDSVMDKKIKDVLNSLEYSPSPISKKLSCASVKS} \\ {\tt QGRPSSCPAGMAVTGCACGYGCGSWDVQLETTCHCQCSVVDWTTARCCHLT} \\$

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FIGURE 415

CAGAAGAGGGGCTAGCTGTCTCTGCGGACCAGGGAGACCCCGGGCCCCCCGGTGTG AGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAGGA GTGTGTGGAACAGGACCCGGGACAGAGGAACCATGGCTCCGCAGAACCTGAGCACCTTTTGCC TGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTGGGGG TGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAAACTAGCCCTGCAGCTTC ATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTGCTGCTT ATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAAGGATTAA AAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTCACACTTCTTTGGGGATTTTTGGTTTCA TGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATATTATTGTAG CTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGATGCGGACCACCC AGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAATGCCCTAATGTCA AACTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTGAGAGACGCCATGG AGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGGAGATTTACGGTTCC GAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATTTGTACACAAATGTGA CAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACTCACTTGGATGGTCACA AGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCTATGGAAGAAAGGGGAAG GGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAATCACTTTTGATGTGGATT TTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAACAGCTACTGAAACAAGGGT CAGTGCAGAAGGTATACAATGGACTGCAAGGATAT**TGA**GAGTGAATAAAATTGGACTTTGTTT TTTTCAATATGCAAGTTAGGCTTAATTTTTTTTATCTAATGATCATCATGAAATGAATAAGAGG GCTTAAGAATTTGTCCATTTGCATTCGGAAAAGAATGACCAGCAAAAGGTTTACTAATACCTC TCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGTTTCAAGAATTAAAGCTGCAAGAGG CCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTTGTTATTTTTA

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FIGURE 416

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQAQEKFQDLGAAYE VLSDSEKRKQYDTYGEEGLKDGHQSSHGDIFSHFFGDFGFMFGGTPRQQDRNIPRGSDIIVDLEVTLEEVYAGNF VEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQMTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGMEYPFI GEGEPHVDGEPGDLRFRIKVVKHPIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLW KKGEGLPNFDNNNIKGSLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

Important features:

Signal peptide:

amino acids 1-22

Cell attachment sequence.

amino acids 254-257

Nt-dnaJ domain signature.

amino acids 67-87

Homologous region to Nt-dnaJ domain proteins.

amino acids 26-58

N-glycosylation site.

amino acids 5-9, 261-265

Tyrosine kinase phosphorylation site.

amino acids 253-260

N-myristoylation site.

amino acids 18-24, 31-37, 93-99, 215-221

Amidation site.

amino acids 164-168

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FIGURE 417

CGGCGGCGCTGCGGGCGAGGTGAGGGGCGCGAGGTGAGGGCGCGAGGTTCCCAGCAGGA GATGACCAAGGCCCGGCTGTTCCGGCTGTGGCTGGTGCTGGGGTCGGTGTTCATGATCCTGCT GATCATCGTGTACTGGGACAGCGCAGGCGCCGCGCACTTCTACTTGCACACGTCCTTCTCTAG GCCGCACACGGGGCCGCCGCTGCCCACGCCCGGGCCGGACAGGGACAGGGAGCTCACGGCCGA CTCCGATGTCGACGAGTTTCTGGACAAGTTTCTCAGTGCTGGCGTGAAGCAGAGCGACCTTCC CAGAAAGGAGACGGAGCAGCCGCCTGCGCCGGGGAGCATGGAGAGAGCGTGAGAGGCTACGA CGTGCTGCGGGGCTTCTGCGCCAACTCCAGCCTGGCCTTCCCCACCAAGGAGCGCGCATTCGA CGACATCCCCAACTCGGAGCTGAGCCACCTGATCGTGGACGACCGGCACGGGGCCATCTACTG CTACGTGCCCAAGGTGGCCTGCACCAACTGGAAGCGCGTGATGATCGTGCTGAGCGGAAGCCT GCTGCACCGCGGTGCGCCCTACCGCGACCCGCTGCGCATCCCGCGCGAGCACGTGCACAACGC CAGCGCGCACCTGACCTTCAACAAGTTCTGGCGCCGCTACGGGAAGCTCTCCCGCCACCTCAT GAAGGTCAAGCTCAAGAAGTACACCAAGTTCCTCTTCGTGCGCGACCCCTTCGTGCGCCTGAT CTCCGCCTTCCGCAGCAAGTTCGAGCTGGAGAACGAGGAGTTCTACCGCAAGTTCGCCGTGCC CATGCTGCGGCTGTACGCCAACCACCAGCCTGCCCGCCTCGGCGCGCGAGGCCTTCCGCGC TGGCCTCAAGGTGTCCTTCGCCAACTTCATCCAGTACCTGCTGGACCCGCACACGGAGAAGCT GGCGCCCTTCAACGAGCACTGGCGGCAGGTGTACCGCCTCTGCCACCCGTGCCAGATCGACTA CGACTTCGTGGGGAAGCTGGAGACTCTGGACGAGGACGCCGCGCAGCTGCTGCAGCTACTCCA GGTGGACCGCCAGCTCCCCCCCGAGCTACCGGAACAGGACCGCCAGCAGCTGGGAGGA GGACTGGTTCGCCAAGATCCCCCTGGCCTGGAGGCAGCCTGTATAAACTCTACGAGGCCGA CTTTGTTCTCTTCGGCTACCCCAAGCCCGAAAACCTCCTCCGAGAC**TGA**AAGCTTTCGCGTTG CTTTTTCTCGCGTGCCTGGAACCTGACGCACGCGCACTCCAGTTTTTTTATGACCTACGATTT TGCAATCTGGGCTTCTTGTTCACTCCACTGCCTCTATCCATTGAGTACTGTATCGATATTGTT TTTTAAGATTAATATTTCAGGTATTTAATACGA

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FIGURE 418

MTKARLFRLWLVLGSVFMILLIIVYWDSAGAAHFYLHTSFSRPHTGPPLPTPGPDRDRELTAD SDVDEFLDKFLSAGVKQSDLPRKETEQPPAPGSMEESVRGYDWSPRDARRSPDQGRQQAERRS VLRGFCANSSLAFPTKERAFDDIPNSELSHLIVDDRHGAIYCYVPKVACTNWKRVMIVLSGSL LHRGAPYRDPLRIPREHVHNASAHLTFNKFWRRYGKLSRHLMKVKLKKYTKFLFVRDPFVRLI SAFRSKFELENEEFYRKFAVPMLRLYANHTSLPASAREAFRAGLKVSFANFIQYLLDPHTEKL APFNEHWRQVYRLCHPCQIDYDFVGKLETLDEDAAQLLQLLQVDRQLRFPPSYRNRTASSWEE DWFAKIPLAWRQQLYKLYEADFVLFGYPKPENLLRD

Important features:

Signal peptide:

amino acids 1-31

N-glycosylation sites.

amino acids 134-137, 209-212, 280-283 and 370-373

TNFR/NGFR family cysteine-rich region protein

amino acids 329-332

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FIGURE 419

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAAG GTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATC**ATG**GACCTCGCGGGACTGCTGA AGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATCATCA ACACCATTCAGCTCTTCACTCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAAGATCA ACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGTCGGCCA TGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGAACGCTTTG GGCTGTTAGGGGGCTCCAAGGTCCTGGCCAAGAAAGAGCTGGCCTATGTCCCAATTATCGGCT GGATGTGGTACTTCACCGAGATGGTCTTCTGTTCGCGCAAGTGGGAGCAGGATCGCAAGACGG TTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCCTGATTCACTGTG AGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCCGGGCCAAGGGGC TGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATCACCGTGAGGAGCT TGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTCAGAAATAATGAAAATCCAA CACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATGTTAGGAGGATCCCAC TGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCACAAGCTCTACCAGGAGA AGGATGCCTTTCAGGAGGAGTACTACAGGACGGCCACCTTCCCAGAGACGCCCATGGTGCCCC CCCGGCGGCCCTGGACCCTCGTGACTGGCTGTTTTTGGGCCTCGCTGGTGCTCTACCCTTTCT TCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACGCTGGCCAGCTTCATCCTCG TCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGACGGAAATTGACAAGGGCT CTGCCTACGGCAACTCTGACAGCAAGCAGAAACTGAATGAC**TGA**CTCAGGGAGGTGTCACCAT CCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCTCCTTAGTGGGACACGGTGACAA CTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTTTTTTCCCCATGTGCTTTAGTGGGC AGTTCCCCTTTCATCCTTTGGTGCTGAGTTTTCTGTAACCCTTGGTTGCCAGAGATAAAGTGA GGGTCAAAAAAAAAAA

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FIGURE 420

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLVM LLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHKFEIDFLCGWSLSERFGLLGGSKVLAKKEL AYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQHLRDYPEKYFFLIHCEGTRFTEKKHEISM QVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVLNGKKYHAD LYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWTLVNWLFWA SLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDSKQKLND

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FIGURE 421

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCTGGGTGCCTGCATC GCC<u>ATG</u>GACACCACCAGGTACAGCAAGTGGGGCGGCAGCTCCGAGGAGGTCCCCGGAGGGCCC TGGGGACGCTGGGTGCACTGGAGCAGGAGACCCCTCTTCTTGGCCCTGGCTGTCCTGGTCACC CTGCTTGACGCCACGACCTGCTGAGGACAAACGCCTCGAAGCAGACGGCGCGCTGGGTGCC CTGAAGGAGGAGGTCGGAGACTGCCACAGCTGCTCCGGGGACGCAGGCGCAGCTGCAGACC ACGCGCGCGGAGCTTGGGGAGGCGCAGGCGAAGCTGATGGAGCAGGAGAGCGCCCTGCGGGAA CTGCGTGAGCGCGTGACCCAGGGCTTGGCTGAAGCCGGCAGGGCCGTGAGGACGTCCGCACT GAGCTGTTCCGGGCGCTGGAGGCCGTGAGGCTCCAGAACAACTCCTGCGAGCCGTGCCCCACG TCGTGGCTGTCCTTCGAGGGCTCCTGCTACTTTTTCTCTGTGCCAAAGACGACGTGGGCGGCG GCGCAGGATCACTGCGCAGATGCCAGCGCGCACCTGGTGATCGTTGGGGGCCTGGATGAGCAG CAGGGAGAGCCCAATGACGCTTGGGGGCGCGAGAACTGTGTCATGATGCTGCACACGGGGCTG TGGAACGACGCACCGTGTGACAGCGAGAAGGACGGCTGGATCTGTGAGAAAAGGCACAACTGC **TGA**CCCCGCCCAGTGCCCTGGAGCCGCCCCATTGCAGCATGTCGTATCCTGGGGGCTGCTCA CCTCCCTGGCTCCTGGAGCTGATTGCCAAAGAGTTTTTTTCTTCCTCATCCACCGCTGCTGAG TCTCAGAAACACTTGGCCCAACATAGCCCTGTCCAGCCCAGTGCCTGGGCTCTGGGACCTCCA TGCCGACCTCATCCTAACTCCACTCACGCAGACCCAACCTAACCTCCACTAGCTCCAAAATCC CTGCTCCTGCGTCCCGTGATATGCCTCCACTTCTCTCCCTAACCAAGGTTAGGTGACTGAGG ACTGGAGCTGTTTGGTTTTCTCGCATTTTCCACCAAACTGGAAGCTGTTTTTGCAGCCTGAGG AAGCATCAATAAATATTTGAGAAATGAAAAAA

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FIGURE 422

MDTTRYSKWGGSSEEVPGGPWGRWVHWSRRPLFLALAVLVTTVLWAVILSILLSKASTERAAL LDGHDLLRTNASKQTAALGALKEEVGDCHSCCSGTQAQLQTTRAELGEAQAKLMEQESALREL RERVTQGLAEAGRGREDVRTELFRALEAVRLQNNSCEPCPTSWLSFEGSCYFFSVPKTTWAAA QDHCADASAHLVIVGGLDEQGFLTRNTRGRGYWLGLRAVRHLGKVQGYQWVDGVSLSFSHWNQ GEPNDAWGRENCVMMLHTGLWNDAPCDSEKDGWICEKRHNC

Important features:

Type II transmembrane domain:

amino acids 31-54

N-glycosylation sites.

amino acids 73-76 and 159-162

Leucine zipper pattern.

amino acids 102-123

N-myristoylation sites.

amino acids 18-23, 133-138 and 242-247

C-type lectin domain signature.

amino acids 264-287

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FIGURE 423

GCGCCGCCAGGCGTAGGCGGGGTGGCCCTTGCGTCTCCCGCTTCCTTGAAAAACCCGGCGGGC GCCCAAC<u>ATG</u>GCGGGTGGGCGCTGCGGCCCGCAGCTAACGGCGCTCCTGGCCGCCTGGATCGC GGCTGTGGCGGCGACGCAGGCCCCGAGGAGGCCGCCGCTGCCGCCGGAGCAGAGCCGGGTCCA GCCCATGACCGCCTCCAACTGGACGCTGGTGATGGAGGGCGAGTGGATGCTGAAATTTTACGC CCCATGGTGTCCATCCTGCCAGCAGACTGATTCAGAATGGGAGGCTTTTGCAAAGAATGGTGA AATACTTCAGATCAGTGTGGGGAAGGTAGATGTCATTCAAGAACCAGGTTTGAGTGGCCGCTT CTTTGTCACCACTCTCCCAGCATTTTTTCATGCAAAGGATGGGATATTCCGCCGTTATCGTGG CCCAGGAATCTTCGAAGACCTGCAGAATTATATCTTAGAGAAGAAATGGCAATCAGTCGAGCC TCTGACTGGCTGGAAATCCCCAGCTTCTCTAACGATGTCTGGAATGGCTGGTCTTTTTAGCAT CTCTGGCAAGATATGGCATCTTCACAACTATTTCACAGTGACTCTTGGAATTCCTGCTTGGTG TTCTTATGTGTTTTTCGTCATAGCCACCTTGGTTTTTTGGCCTTTTTATGGGTCTGGTCTTGGT GGTAATATCAGAATGTTTCTATGTGCCACTTCCAAGGCATTTATCTGAGCGTTCTGAGCAGAA TCGGAGATCAGAGGAGGCTCATAGAGCTGAACAGTTGCAGGATGCGGAGGAGGAAAAAGATGA TTCAAATGAAGAAGAAAACAAAGACAGCCTTGTAGATGATGAAGAAGAAGAAGAAGATCTTGG CGATGAGGATGAAGCAGAGGAAGAAGAGGAGGAGACAACTTGGCTGCTGGTGTGGATGAGGA GAGAAGTGAGGCCAATGATCAGGGGCCCCCAGGAGAGGACGGTGTGACCCGGGAGGAAGTAGA GCCTGAGGAGGCTGAAGAAGGCATCTCTGAGCAACCCTGCCCAGCTGACACAGAGGTGGTGGA AGACTCCTTGAGGCAGCGTAAAAGTCAGCATGCTGACAAGGGACTG**TAG**ATTTAATGATGCGT TTTCAAGAATACACCAAAACAATATGTCAGCTTCCCTTTGGCCTGCAGTTTGTACCAAATC CTTAATTTTTCCTGAATGAGCAAGCTTCTCTTAAAAGATGCTCTCTAGTCATTTGGTCTCATG GCAGTAAGCCTCATGTATACTAAGGAGAGTCTTCCAGGTGTGACAATCAGGATATAGAAAAAAC GAGAGTCTCGACCAGAGGGGGCCATTCCCAGTCCTAATCAGCACCTTCCAGAGACAAGGCTGC AGGCCCTGTGAAATGAAAGCCAAGCAGGAGCCTTGGCTCCTGAGCATCCCCAAAGTGTAACGT AGAAGCCTTGCATCCTTTTCTTGTGTAAAGTATTTATTTTTGTCAAATTGCAGGAAACATCAG GCACCACAGTGCATGAAAAATCTTTCACAGCTAGAAATTGAAAGGGCCTTGGGTATAGAGAGC AGCTCAGAAGTCATCCCAGCCCTCTGAATCTCCTGTGCTATGTTTTATTTCTTACCTTTAATT TTTCCAGCATTTCCACCATGGGCATTCAGGCTCTCCACACTCTTCACTATTATCTCTTGGTCA AGATAATCAGTAACCATAACCCCTGAAGCTGTGACTGCCAAACATCTCAAATGAAATGTTGTG CCAAAATATAGTTGTTGATTTTTTTTTTAAGTTTTCTAAGCAATATTTTTCAAGCCAGAAG TCCTCTAAGTCTTGCCAGTACAAGGTAGTCTTGTGAAGAAAAGTTGAATACTGTTTTGTTTTC ATCTCAAGGGGTTCCCTGGGTCTTGAACTACTTTAATAATAACTAAAAAACCACTTCTGATTT TCCTTCAGTGATGTGCTTTTGGTGAAAGAATTAATGAACTCCAGTACCTGAAAGTGAAAGATT TGATTTTGTTTCCATCTTCTGTAATCTTCCAAAGAATTATATCTTTGTAAATCTCTCAATACT CAATCTACTGTAAGTACCCAGGGAGGCTAATTTCTTT

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FIGURE 424

MAGGRCGPQLTALLAAWIAAVAATAGPEEAALPPEQSRVQPMTASNWTLVMEGEWMLKFYAPW
CPSCQQTDSEWEAFAKNGEILQISVGKVDVIQEPGLSGRFFVTTLPAFFHAKDGIFRRYRGPG
IFEDLQNYILEKKWQSVEPLTGWKSPASLTMSGMAGLFSISGKIWHLHNYFTVTLGIPAWCSY
VFFVIATLVFGLFMGLVLVVISECFYVPLPRHLSERSEQNRRSEEAHRAEQLQDAEEEKDDSN
EEENKDSLVDDEEEKEDLGDEDEAEEEEEEDNLAAGVDEERSEANDQGPPGEDGVTREEVEPE
EAEEGISEQPCPADTEVVEDSLRQRKSQHADKGL

Important features:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 191-211

N-glycosylation site.

amino acids 46-49

Thioredoxin family proteins. (homologous region to disulfide isomerase) amino acids 56-72

Flavodoxin proteins

amino acids 173-187

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FIGURE 425

GAGGAACCTACCGGTACCGGCCGCGCGCTGGTAGTCGCCGGTGTGGCTGCACCTCACCAATCCCGTGCGCCGCGG CTGGGCCGTCGGAGAGTGCGTGTGCTTCTCCTGCACGCGGTGCTTGGGCTCGGCCAGGCGGGGTCCGCCGCCA GGGTTTGAGGATGGGGGGAGTAGCTACAGGAAGCGACCCCGCGATGGCAAGGTATATTTTTGTGGAATGAAAAGGA AGTATTAGAAATGAGCTGAAGACCATTCACAGATTAATATTTTTGGGGACAGATTTGTGATGCTTGATTCACCCT TGAAGTAATGTAGACAGAAGTTCTCAAATTTGCATATTACATCAACTGGAACCAGCAGTGAATCTTAATGTTCAC GATCATTCTCTGTTTTCTGATAGTGTATATGGCCATTTTAGTGGGCACAGATCAGGATTTTTACAGTTTACTTGG AGTGTCCAAAACTGCAAGCAGTAGAGAAATAAGACAAGCTTTCAAGAAATTGGCATTGAAGTTACATCCTGATAA TCTACGGAAAAAGTATGACAAATATGGAGAAAAGGGACTTGAGGATAATCAAGGTGGCCAGTATGAAAGCTGGAA CTATTATCGTTATGATTTTGGTATTTATGATGATGATCCTGAAATCATAACATTGGAAAGAAGAAGAATTTGATGC TGCTGTTAATTCTGGAGAACTGTGGTTTGTAAATTTTTACTCCCCAGGCTGTTCACACTGCCATGATTTAGCTCC CACATGGAGAGACTTTGCTAAAGAAGTGGATGGGTTACTTCGAATTGGAGCTGTTAACTGTGGTGATGATAGAAT GCTTTGCCGAATGAAAGGAGTCAACAGCTATCCCAGTCTCTTCATTTTTCGGTCTGGAATGGCCCCAGTGAAATA TCATGGAGACAGATCAAAGGAGAGTTTAGTGAGTTTTGCAATGCAGCATGTTAGAAGTACAGTGACAGAACTTTG AGGAGGAGATTGTTTGACTTCACAGACACGACTCAGGCTTAGTGGCATGTTGTTTCTCAACTCATTGGATGCTAA AGAAATATATTTGGAAGTAATACATAATCTTCCAGATTTTGAACTACTTTCGGCAAACACACTAGAGGATCGTTT GGCTCATCATCGGTGGCTGTTATTTTTTCATTTTGGAAAAATGAAAATTCAAATGATCCTGAGCTGAAAAAACT AAAAACTCTACTTAAAAATGATCATATTCAAGTTGGCAGGTTTGACTGTTCCTCTGCACCAGACATCTGTAGTAA TCTGTATGTTTTCAGCCGTCTCTAGCAGTATTTAAAGGACAAGGAACCAAAGAATATGAAATTCATCATGGAAA GAAGATTCTATATGATATACTTGCCTTTGCCAAAGAAAGTGTGAATTCTCATGTTACCACGCTTGGACCTCAAAA TTTTCCTGCCAATGACAAAGAACCATGGCTTGTTGATTTCTTTGCCCCCTGGTGTCCACCATGTCGAGCTTTACT ACCAGAGTTACGAAGAGCATCAAATCTTCTTTATGGTCAGCTTAAGTTTGGTACACTAGATTGTACAGTTCATGA GGGACTCTGTAACATGTATAACATTCAGGCTTATCCAACAACAGTGGTATTCAACCAGTCCAACATTCATGAGTA TGAAGGACATCACTCTGCTGAACAAATCTTGGAGTTCATAGAGGATCTTATGAATCCTTCAGTGGTCTCCCTTAC ACCCACCACCTTCAACGAACTAGTTACACAAAGAAAACACCAACGAAGTCTGGATGGTTGATTTCTATTCTCCGTG GTGTCATCCTTGCCAAGTCTTAATGCCAGAATGGAAAAGAATGGCCCGGACATTAACTGGACTGATCAACGTGGG CAGTATAGATTGCCAACAGTATCATTCTTTTTGTGCCCAGGAAAACGTTCAAAGATACCCTGAGATAAGATTTTT TCCCCCAAAATCAAATAAAGCTTATCAGTATCACAGTTACAATGGTTGGAATAGGGATGCTTATTCCCTGAGAAT CTGGGGTCTAGGATTTTTACCTCAAGTATCCACAGATCTAACACCTCAGACTTTCAGTGAAAAAGTTCTACAAGG GAAAAATCATTGGGTGATTGATTTCTATGCTCCTTGGTGTGGACCTTGCCAGAATTTTGCTCCAGAATTTGAGCT CTTGGCTAGGATGATTAAAGGAAAAGTGAAAGCTGGAAAAGTAGACTGTCAGGCTTATGCTCAGACATGCCAGAA AGCTGGGATCAGGGCCTATCCAACTGTTAAGTTTTATTTCTACGAAAGAGCAAAGAGAAATTTTCAAGAAGAGCA GATAAATACCAGAGATGCAAAAGCAATCGCTGCCTTAATAAGTGAAAAATTGGAAACTCTCCGAAATCAAGGCAA GAGGAATAAGGATGAACTT<u>TGA</u>TAATGTTGAAGATGAAGAAAAAGTTTAAAAGAAATTCTGACAGATGACATCAG GAATTATCTACAGCACTGGTGTAAAAGAAGGGTCTGCAAACTTTTTCTGTAAAGGGCCGGTTTATAAATATTTTA GACTTTGCAGGCTATAATATATGGTTCACACATGAGAACAAGAATAGAGTCATCATGTATTCTTTGTTATTTGCT TTTAACAACCTTTAAAAAATATTAAAACGATTCTTAGCTCAGAGCCATACAAAAGTAGGCTGGATTCAGTCCATG ATCTACATAAATGTCTAAGTTGTATAAAGTCCACTTTCCCTTCACGTTTTTTTGGCTGACCTGAAAAGAGGTAACT TAGTTTTTGGTCACTTGTTCTCCTAAAAATGCTATCCCTAACCATATATTTATATTTCGTTTTAAAAAACACCCAT TAGCAATTAACTGGGCATTGTAGAGTATCCTAAATATGTTATCAAGTATTTAGAGTTCTATATTTTAAAGATATA TGTGTTCATGTATTTCTGAAATTGCTTTCATAGAAATTTTCCCACTGATAGTTGATTTTTTGAGGCATCTAATAT TTTTTCACTCCTGTCCAGTCTATTTATTATTCAAATAGGAAAAATTACTTTACAGGTTGTTTTACTGTAGCTTAT AATGATACTGTAGTTATTCCAGTTACTAGTTTACTGTCAGAGGGCTGCCTTTTTCAGATAAATATTGACATAATA ACTGAAGTTATTTTATAAGAAAATCAAGTATATAAATCTAGGAAAGGGATCTTCTAGTTTCTGTGTTTTTAGA CTCAAAGAATCACAAATTTGTCAGTAACATGTAGTTGTTTAGTTATAATTCAGAGTGTACAGAATGGTAAAAATT

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FIGURE 426

MGVWLNKDDYIRDLKRIILCFLIVYMAILVGTDQDFYSLLGVSKTASSREIRQAFKKLALKLH
PDKNPNNPNAHGDFLKINRAYEVLKDEDLRKKYDKYGEKGLEDNQGGQYESWNYYRYDFGIYD
DDPEIITLERREFDAAVNSGELWFVNFYSPGCSHCHDLAPTWRDFAKEVDGLLRIGAVNCGDD
RMLCRMKGVNSYPSLFIFRSGMAPVKYHGDRSKESLVSFAMQHVRSTVTELWTGNFVNSIQTA
FAAGIGWLITFCSKGGDCLTSQTRLRLSGMLFLNSLDAKEIYLEVIHNLPDFELLSANTLEDR
LAHHRWLLFFHFGKNENSNDPELKKLKTLLKNDHIQVGRFDCSSAPDICSNLYVFQPSLAVFK
GQGTKEYEIHHGKKILYDILAFAKESVNSHVTTLGPQNFPANDKEPWLVDFFAPWCPPCRALL
PELRRASNLLYGQLKFGTLDCTVHEGLCNMYNIQAYPTTVVFNQSNIHEYEGHHSAEQILEFI
EDLMNPSVVSLTPTTFNELVTQRKHNEVWMVDFYSPWCHPCQVLMPEWKRMARTLTGLINVGS
IDCQQYHSFCAQENVQRYPEIRFFPPKSNKAYQYHSYNGWNRDAYSLRIWGLGFLPQVSTDLT
PQTFSEKVLQGKNHWVIDFYAPWCGPCQNFAPEFELLARMIKGKVKAGKVDCQAYAQTCQKAG
IRAYPTVKFYFYERAKRNFQEEQINTRDAKAIAALISEKLETLRNQGKRNKDEL

Important features:

Endoplasmic reticulum targeting sequence.

amino acids 744-747

Cytochrome c family heme-binding site signature.

amino acids 158-163

Nt-dnaJ domain signature.

amino acids 77-96

N-glycosylation site.

amino acids 484-487

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FIGURE 427

CTGCAGTCAGGACTCTGGGACCGCAGGGGGCTCCCGGACCCTGACTCTGCAGCCGAACCGGCA GTCCTTCTGAGATGATGGCTCTGGGCGCAGCGGGAGCTACCCGGGTCTTTGTCGCGATGGTAG CGGCGGCTCTCGGCGGCCACCCTCTGCTGGGAGTGAGCGCCACCTTGAACTCGGTTCTCAATT CCAACGCTATCAAGAACCTGCCCCCACCGCTGGGCGGCGCTGCGGGGCACCCAGGCTCTGCAG TCAGCGCCGCGCGGGAATCCTGTACCCGGGCGGGAATAAGTACCAGACCATTGACAACTACC AGCCGTACCCGTGCGCAGAGGACGAGGAGTGCGGCACTGATGAGTACTGCGCTAGTCCCACCC GCGGAGGGGACGCAGGCGTGCAAATCTGTCTCGCCTGCAGGAAGCGCCGAAAACGCTGCATGC GTCACGCTATGTGCTGCCCCGGGAATTACTGCAAAAATGGAATATGTGTGTCTTCTGATCAAA ATCATTTCCGAGGAGAATTGAGGAAACCATCACTGAAAGCTTTGGTAATGATCATAGCACCT TGGATGGGTATTCCAGAAGAACCACCTTGTCTTCAAAAATGTATCACACCAAAGGACAAGAAG GTTCTGTTTGTCTCCGGTCATCAGACTGTGCCTCAGGATTGTGTTGTTGCTAGACACTTCTGGT CCAAGATCTGTAAACCTGTCCTGAAAGAAGGTCAAGTGTGTACCAAGCATAGGAGAAAAGGCT AAGATCACCATCAAGCCAGTAATTCTTCTAGGCTTCACACTTGTCAGAGACACTAAACCAGCT ATCCAAATGCAGTGAACTCCTTTTATATAATAGATGCTATGAAAACCTTTTATGACCTTCATC AACTCAATCCTAAGGATATACAAGTTCTGTGGTTTCAGTTAAGCATTCCAATAACACCTTCCA AAAACCTGGAGTGTAAGAGCTTTGTTTCTTTATGGAACTCCCCTGTGATTGCAGTAAATTACT GTATTGTAAATTCTCAGTGTGGCACTTACCTGTAAATGCAATGAAACTTTTAATTATTTTTCT CTTGACTGACAAATATTCTATATTGAACTGAAGTAAATCATTTCAGCTTATAGTTCTTAAAAG CATAACCCTTTACCCCATTTAATTCTAGAGTCTAGAACGCAAGGATCTCTTGGAATGACAAAT GATAGGTACCTAAAATGTAACATGAAAATACTAGCTTATTTTCTGAAATGTACTATCTTAATG CTTAAATTATATTTCCCTTTAGGCTGTGATAGTTTTTGAAATAAAATTTAACATTTAAAAAAA AAAAA

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FIGURE 428

MMALGAAGATRVFVAMVAAALGGHPLLGVSATLNSVLNSNAIKNLPPPLGGAAGHPGSAVSAA PGILYPGGNKYQTIDNYQPYPCAEDEECGTDEYCASPTRGGDAGVQICLACRKRRKRCMRHAM CCPGNYCKNGICVSSDQNHFRGEIEETITESFGNDHSTLDGYSRRTTLSSKMYHTKGQEGSVC LRSSDCASGLCCARHFWSKICKPVLKEGQVCTKHRRKGSHGLEIFQRCYCGEGLSCRIQKDHH QASNSSRLHTCQRH

Important features:

Signal peptide:

amino acids 1-23

N-glycosylation site.

amino acids 256-259

Fungal Zn(2)-Cys(6) binuclear cluster domain

amino acids 110-126

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FIGURE 429

GAGAGGACGAGGTGCCGCTGCAGAGAATCCTCCGCTGCCGTCGGCTCCCGGAGCCCAGCCC TTTCCTAACCCAACCCAACCTAGCCCAGTCCCAGCCGCAGCGCCTGTCCCTGTCACGGACCC CAGCGTTACCATGCATCCTGCCGTCTTCCTATCCTTACCCGACCTCAGATGCTCCCTTCTGCT CCTGGTAACTTGGGTTTTTACTCCTGTAACAACTGAAATAACAAGTCTTGCTACAGAGAATAT AGATGAAATTTTAAACAATGCTGATGTTGCTTTAGTAAATTTTTATGCTGACTGGTGTCGTTT CAGTCAGATGTTGCATCCAATTTTTGAGGAAGCTTCCGATGTCATTAAGGAAGAATTTCCAAA TGAAAATCAAGTAGTGTTTGCCAGAGTTGATTGTGATCAGCACTCTGACATAGCCCAGAGATA CAGGATAAGCAAATACCCAACCCTCAAATTGTTTCGTAATGGGATGATGATGAAGAGAGAAATA CAGGGGTCAGCGATCAGTGAAAGCATTGGCAGATTACATCAGGCAACAAAAAAGTGACCCCAT TCAAGAAATTCGGGACTTAGCAGAAATCACCACTCTTGATCGCAGCAAAAGAAATATCATTGG ATATTTTGAGCAAAAGGACTCGGACAACTATAGAGTTTTTTGAACGAGTAGCGAATATTTTGCA TGATGACTGTGCCTTTCTTCTGCATTTGGGGATGTTTCAAAACCGGAAAGATATAGTGGCGA CAACATAATCTACAAACCACCAGGGCATTCTGCTCCGGATATGGTGTACTTGGGAGCTATGAC AAATTTTGATGTGACTTACAATTGGATTCAAGATAAATGTGTTCCTCTTGTCCGAGAAATAAC ATTTGAAAATGGAGAGGAATTGACAGAAGAAGGACTGCCTTTTCTCATACTCTTTCACATGAA AGAAGATACAGAAAGTTTAGAAATATTCCAGAATGAAGTAGCTCGGCAATTAATAAGTGAAAA AGGTACAATAAACTTTTTACATGCCGATTGTGACAAATTTAGACATCCTCTTCTGCACATACA AGACTTCAAAGATGTATTAATTCCTGGAAAACTCAAGCAATTCGTATTTGACTTACATTCTGG AAAACTGCACAGAGAATTCCATCATGGACCTGACCCAACTGATACAGCCCCAGGAGAGCCAAGC CCAAGATGTAGCAAGCAGTCCACCTGAGAGCTCCTTCCAGAAACTAGCACCCAGTGAATATAG GTATACTCTATTGAGGGATCGAGATGAGCTT**TAA**AAACTTGAAAAACAGTTTGTAAGCCTTTC AACAGCAGCATCAACCTACGTGGTGGAAATAGTAAACCTATATTTTCATAATTCTATGTGTAT AAAAAAAAA

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FIGURE 430

MHPAVFLSLPDLRCSLLLLVTWVFTPVTTEITSLATENIDEILNNADVALVNFYADWCRFSQM LHPIFEEASDVIKEEFPNENQVVFARVDCDQHSDIAQRYRISKYPTLKLFRNGMMMKREYRGQ RSVKALADYIRQQKSDPIQEIRDLAEITTLDRSKRNIIGYFEQKDSDNYRVFERVANILHDDC AFLSAFGDVSKPERYSGDNIIYKPPGHSAPDMVYLGAMTNFDVTYNWIQDKCVPLVREITFEN GEELTEEGLPFLILFHMKEDTESLEIFQNEVARQLISEKGTINFLHADCDKFRHPLLHIQKTP ADCPVIAIDSFRHMYVFGDFKDVLIPGKLKQFVFDLHSGKLHREFHHGPDPTDTAPGEQAQDV ASSPPESSFQKLAPSEYRYTLLRDRDEL

Important features:

Signal peptide:

amino acids 1-29

Endoplasmic reticulum targeting sequence.

amino acids 403-406

Tyrosine kinase phosphorylation site.

amino acids 203-211

Thioredoxin family proteins

amino acids 50-66

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FIGURE 431

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGCA GGCTGCTGCTGCTGCTTCGCGGAGGGCGCAGGCCCTGGAGTGCTACAGCTGCGTG GACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGCAGTG CGGGGTTGCGGTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGCTTCTG GCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTCACCTCG ${\tt CGGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCAACGGCGTGGAGTGCTACAGC}$ TGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCGTGAGCTGCTACAAC GCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTCACCTTGACGGCAGCTAATGTG ACTGTGTCCTGCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGATGGAGTAACA GGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAACTCTGACCTCCGC AACAAGACCTACTTCTCCCCTCGAATCCCACCCCTTGTCCGGCTGCCCCCTCCAGAGCCCACG ACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAGACCCACATCCACC ACCAAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAGAACACGAGGCCTCC CGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGACCGCAGCAATTCAGGG CAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCATAATAAAGGCTGTGTGGCTCCCACAGCT GGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCCTACTG**TGA**GCTTCTCCACCTGGA AATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCTCATCACTTCCTGTTCCCA CCACTGGACTGGCCCAGCCCCTGTTTTTCCAACATTCCCCAGTATCCCCAGCTTCTGC TGCGCTGGTTTGCGGCTTTGGGAAATAAAATACCGTTGTATATATTCTGCCAGGGGTGTTCTA GCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTCTCCGCTTGTCCTCTTGTGATG ACTCTAAGCACTGCCTCCCCTACTCCCGCATCTTTGGGGAATCGGTTCCCCATATGTCTTCC TTACTAGACTGTGAGCTCCTCGAGGGGGGCCCGGTACCCAATTCGCCCTATAGTGAGTCGTA

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FIGURE 432

MDPARKAGAQAMIWTAGWLLLLLRGGAQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCTE
AVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNAKLNLTSRALDP
AGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCFDGNVTLTAANVTVSLP
VRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPPLVRLPPPEPTTVAST
TSVTTSTSAPVRPTSTTKPMPAPTSQTPRQGVEHEASRDEEPRLTGGAAGHQDRSNSGQYPAK
GGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

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FIGURE 433

CGGGACTCGGCGGGTCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCC<u>ATG</u>GAGTT GGTGCTGGTCTTCCTCTGCAGCCTGCTGGCCCCCATGGTCCTGGCCAGTGCAGCTGAAAAGGA GAAGGAAATGGACCCTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGTTCGC TGTGGTCCTCTTCTCGGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTTTCAA TCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCCAATGC AACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAACCTGAG GCGGCTGCTTGAACCTTTGGATGCAAATGTCGATGCT**TAA**GAAAACCGGCCACTTCAGCAACA GCCCTTTCCCCAGGAGAAGCCAAGAACTTGTGTGTCCCCCACCCTATCCCCTCTAACACCATT CCTCCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGGTCCTGCCCACCTC CCGTGATGTGTGTGTGTGTGTGTGTGTGTGTGTGTTTTGCTAACTGTGGTCTTTGTGG GCTGAGCCACATGGCCATCTGCTCCTGCCCCGTGGCCCTCCATCACCTTCTGCTCCTA GGAGGCTGCTTGTTGCCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGCGTAGGGTAAGAGC ACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCACTTTGTCATCATTCT TCATGGACTCCTTTCACTCCTTTAACAAAAACCTTGCTTCCTTATCCCACCTGATCCCAGTCT GAAGGTCTCTTAGCAACTGGAGATACAAGGAGCAGGGGTGAGCCCAGCGTTGACGTCAGG CAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGGCTTCCACGAGGAGTCCCCATCTGCC CCGCCCTTCACAGAGCGCCCGGGGATTCCAGGCCCAGGGCTTCTACTCTGCCCCTGGGGAAT GTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGGGACCCTACCCCTTCCAACC TTCCCTGCTTCTGAGACTTCAATCTACAGCCCAGCTCATCCAGATGCAGACTACAGTCCCTGC AATTGGGTCTCTGGCAGGCAATAGTTGAAGGACTCCTGTTCCGTTGGGGCCAGCACACCGGGA TGGATGGAGGGAGAGCCTTTGCTTCTCTGCCTACGTCCCCTTAGATGGGCAGCAGAG GCAACTCCCGCATCCTTTGCTCTGCCTGTCGGTGGTCAGAGCGGTGAGCGAGGTGGGTTGGAG ACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAGGTTGAAGGTCATAACGAGAGTGGG GCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTATCCTCAACAACAACAGAAAAAAAGGAAT AAAATATCCTTTGTTTCCT

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FIGURE 434

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRRCKC SFNQKPRAPGDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRLLEPLDANVDA

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FIGURE 435

GGTCCTTA**ATG**GCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTGC TGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTTTTGCTATGACATCACCGTCA TCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGACTT TTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGGAAGAAACTAA ATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACTTACAG AGCAACTGCGTGACATTCAGCTGGAGAATTACACACCCAAGGAACCCCTCACCCTGCAGGCAA GGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGTTTCGATG GGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCCTGGAGCCA GAAAGATGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATTACTTCTCAA TGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACACCCCTGGAGCCAA GTGCAGGAGCACCACTCGCCATGTCCTCAGGCACAACCCAACTCAGGGCCACAGCCACCACCC TCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCATCTGAGGAGAGT CCTTTAGAGTGACAGGTTAAAGCTGATACCAAAAGGCTCCTGTGAGCACGGTCTTGATCAAAC TCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGTGGCCTCCAGCAGAT CATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCTTTTGCCAACAATTTTA CCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGCTACCTGATGGAATTCCTGCA TCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATTGTCAGTAAAATAATCACG TTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAGAATTTTTAAATTATTTAAT AAGAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTATTGTTCTGTACTGATATTTAA ATAAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAAA

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FIGURE 436

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFLH YDCGNKTVTPVSPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQARMS CEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFSMGD CIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

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FIGURE 437

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAGCTCTTGTGGCAGG TAACTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTCGTCTACCTCACGGCGCAAGTGTGGATTCTGT GTGCAGCCATCGCTGCCGCCTCAGCCGGGCCCCAGAACTGCCCCTCCGTTTGCTCGTGCAGTAACCAGTTCA GCAAGGTGGTGTGCACGCGCGGGGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACC TCATGGAGAACAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCTGGAGGTCCTGCAGTTGG GCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAACACCCTGGAGCTGTTCG ACAACTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTCCAAGCTGCGGGAGCTCTGGCTTCGCAACA ACCCCATCGAAAGCATCCCCTCTTACGCCTTCAACCGGGTGCCCTCCTCATGCGCCTGGACTTGGGGGAGCTCA AGAAGCTGGAGTATATCTCTGAGGGAGCTTTTGAGGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCA ACATTAAAGACATGCCCAATCTCACCCCCCTGGTGGGGGTGGAGGGGGTGGAGATGTCAGGGAACCACTTCCCTG AGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTCATGAACTCACAGGTCAGCCTGA TTGAGCGGAATGCTTTTGACGGGCTGGCTTCACTTGTGGAACTCAACTTGGCCCACAATAACCTCTCTTCTTTGC CCCATGACCTCTTTACCCCGCTGAGGTACCTGGTGGAGTTGCATCTACACCACAACCCTTGGAACTGTGATTGTG ACATTCTGTGGCTAGCCTGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTC CCATGCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCTTCATCATGG ACGCACCTCGAGACCTCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGTCGGACTCCCCCTATGTCCTCCG TGAAGTGGTTGCCCAATGGGACAGTGCTCAGCCACGCCTCCCGCCACCCAAGGATCTCTGTCCTCAACGACG ACTCCAACGCCTCGGCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACTACAGCTTCTTCACCACAG TAACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCCTACCACGTCCACTG GTTACCAGCCGCATATACCACCTCTACCACGGTGCTCATTCAGACTACCCGTGTGCCCAAGCAGGTGGCAGTAC CCGCGACAGACACCACTGACAAGATGCAGACCAGCCTGGATGAAGTCATGAAGACCACCAAGATCATTGGCT GCTTTGTGGCAGTGACTCTGCTAGCTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGC GGAGTACAGTCACAGCCGCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGCAG CAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGGCAGTAGTGCCCCCACAATTCATGACCATATTAACT ACAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGCCTGGGGAACTCTCTGCACCCCACAGTCA CCACTATCTCTGAACCTTATATATATCAGACCCATACCAAGGACAAGGTACAGGAAACTCAAATATGACCCCT CCCCCAAAAAACTTATAAAATGCAATAGAATGCACACAAAGACACTTTTGTACAGAGTGGGGAGAGACTTT **AGTCAAAACA**

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FIGURE 438

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCTR
RGLSEVPQGIPSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLASLN
TLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEYISE
GAFEGLFNLKYLNLGMCNIKDMPNLTPLVGLEELEMSGNHFPEIRPGSFHGLSSLKKLWVMNS
QVSLIERNAFDGLASLVELNLAHNNLSSLPHDLFTPLRYLVELHLHHNPWNCDCDILWLAWWL
REYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAELKCRTPP
MSSVKWLLPNGTVLSHASRHPRISVLNDGTLNFSHVLLSDTGVYTCMVTNVAGNSNASAYLNV
STAELNTSNYSFFTTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQTTRVPKQV
AVPATDTTDKMQTSLDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRSTVTAARTVE
IIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTENSLGNSLHPT
VTTISEPYIIQTHTKDKVOETOI

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FIGURE 439

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGAGGCTG
TCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCTGC
CCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTCCAA
GTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTGCACC
GATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAAGTCCTGGTGGAAATAGTGAAAAAAAT
GTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACCCTGATC
TTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

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FIGURE 440

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEVK HCTDQISFKKRLSLKKSWWK

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FIGURE 441

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FIGURE 442

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDGG QAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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FIGURE 443

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTCG TGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAATATGAACACGTGGCTGCTGTTC CTCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTGCTC CTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCTGAGT ATGTCCCCCACCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATCTTACA CCTCTACTTGAGTATGTCCCTAACCCTGAGCCCCCACGCCTGGGGCCAGAGTCTTTGTCCCC CGTGTGCGCATGTGTTCAGGGTCAGCCTCTCCCAGAAGTGAGATCATGGACAAAAAAGGGCAAA TCACAGGAAGAATTAAATCCATGAGGACCCAGCAGGCCCAGCAAGAAGCTGAACTCACGCCG AGACCTGCAGGAGTGGTGCCAGGTGCT<u>TGA</u>AGTAACAAGTTTAAAATGTTCAGAGACAATGGA ATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTTCCAAAAACAC AAGTAGAAATTCTAACAATGAAATATATTACAGGCAGGTCACCCACTAACCAAACAACTGAAG GAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGTAACAACAACCTCC CTGCTCCTGGCACCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCGTCTTCCATTCTCTG GGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGACACGGGCAGCAGAGTG TGTCCAGGCCAGCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCAACCCCTGGTCAGGGCA TTGTGGCAAGAACGCCCAGCTCAGAATGAACACCCCCACCAAGAGCCTCCTTGTTCATAACC ACAGGTTACCCTACAAACCACTGTCCCCACACACCCTGGGGATGTTTTAAAACCACACCTC AAAAAAAA

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FIGURE 444

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLLDFLGLVHLGQLLIFHIYLSMSPTLSPRSPQGWV VRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQAQ QEAELTPRPAGVVPGA

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FIGURE 445

AGGCGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACCTGGCCTCACAACCTGC
TGTTTCTTCTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAAGA
GGAAGGGGCAAGGGCGGCCTGGGCCCCTGGCCCTCACCAGGTGCCACTGGACCTGG
TGTCACGGATGAAACCGTATGCCCGCATGGAGGAGTATGAGAGGAACATCGAGGAGATGGTG
CCCAGCTGAGGAACAGCTCAGAGCTGGCCCAGAGAAAGTGTGAGGTCAACTTGCAGCTGTGGA
TGTCCAACAAGAGGAGCCTGTCTCCCTGGGGCTACAGCATCAACCACGACCCCAGCCGTATCC
CCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTGGGCTGTGTAACCCCTTCACCATGCAGG
AGGACCGCAGCATGGTGAGCGTGCCGGTGTTCAGCCAGGTTCCTTGCGCCGCCGCCTCTGCC
CGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCGCTGTGGGCT
GCACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCGAGACCATCCTCCT
TGCACCTTTGTGCCAAGAAAGGCCTATGAAAAGTAAACACTGACTTTTGAAAGCAAG

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FIGURE 446

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEYE RNIEEMVAQLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGC VNPFTMQEDRSMVSVPVFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 75-78

Homologous region to IL-17

amino acids 96-180.

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FIGURE 447

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACCATG TGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCTAT CACTCAGCTTCTCCACACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGGTGC CCAAGCCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTGGATG GAGATACCAACACACCCAGGAGGTGGTACAATACAACTGGGAGACTGGGGATGACCGGT TCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAAACTGTGGAAGAACCAG GGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAAGGACTAC TGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAAGCGGTTGA TGGAGAAGGCTTCCCTCCCCTCCCTTGGGGCTTTGTGGCAAAAATCCTATGGTTATCC CTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCTACTAACAGAC TTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACTGAGCGCCTTTGCTGCTGTTTCCTCT GTCCTGTCAGGTCTCCTGGGGATGGTGGCCCACATGATGTATTCACAAGTCTTCCAAGCGACT GTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTGGGCCTTCTACATG GCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCAACACGTACACCAGG ATGGTGCTGGAGTTCAAGTGCAAGCA**TAG**TAAGAGCTTCAAGGAAAACCCGAACTGCCTACCA CATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCCACCGTGGGTCCTTTGACC AGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGGGAGTCGACTTCTACTCC GAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTGAAAGAAGCAGTTAGGTCA TCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGGAGTAGGCTTGAGCCCTACCT TACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCGTCTCTTGAGCATGGTTTTTA GAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTCCTAAGGGATTCCTGGGTGCCA TTCCCTTCTTTACTGATAGTTTCTGTGCCAGGTTCTGGGCTAAACCATGGAGATAAAAAGAAG AGTAAAATACACTTCCCGACCTTAAGGATCTGAAA

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FIGURE 448

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMPV
SLDGDTNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKRGE
KGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQLPPA
TNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSDCQLGSRRLETTCLELWLG
LLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

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FIGURE 449

TGTGCGCCTGCCAGATCCGCCGGCCGCGGACCGGGGCTGCCTCGGAAACACAGAGGGGTCTTCTCTCGCCCTGCA TATAATTAGCCTGCACACAAAGGGAGCAGCTGAATGGAGGTTGTCACTCTCTGGAAAAGGATTTCTGACCGAGCG

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FIGURE 450

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPHN
LSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNHICSVQGDAFQKLRRVKELTLSSNQIT
QLPNTTFRPMPNLRSVDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRSLKF
LDIGYNQLKSLARNSFAGLFKLTELHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIVVSSL
DWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLTSITLAGNL
WDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDAVYAFHLCEDGAEPTSGHLLSAV
TNRSDLGPPASSATTLADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMALIFSFLI
VVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNHIEGALVII
NEYGSCTCHQQPARECEV

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FIGURE 451

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCTCCAGTCACCCTCCCGCCGTTAC AAATTTATCTTGGTGTCCTTCATACTTGCTGCACTGAGTCTTTCAACCACCTTTTCTCTCCAA CTAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACTTATATAAA GTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGTTACTAAT GTTTTTATTACAAAAACCTACCCTAACCATTATACTTTGGTAACTGGCCTCTTTGCAGAGAAT CATGGGATTGTTGCAAATGATATGTTTGATCCTATTCGGAACAAATCTTTCTCCTTGGATCAC ATGAATATTTATGATTCCAAGTTTTGGGAAGAAGCGACACCAATATGGATCACAAACCAGAGG GCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGAACAGATGTAAAAATACATAAGCGCTTT CCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAGAGTTGCCAAAATTGTT GAATGGTTTACGTCAAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGAAGACCCTGATGAC ATGGGCCACCATTTGGGACCTGACAGTCCGCTCATGGGGCCTGTCATTTCAGATATTGACAAG AAGTTAGGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAACACTCTGAACCTAATC ATCACAAGTGATCATGGAATGACGCAGTGCTCTGAGGAAAGGTTAATAGAACTTGACCAGTAC CTGGATAAAGACCACTATACCCTGATTGATCAATCTCCAGTAGCAGCCATCTTGCCAAAAGAA GGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCTCATCCTAATCTTACTGTTTACAAA AAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCGAATTCAACCAATCATAGCA GTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATGACTTTCTGTTAGGCAACCAC GGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTTAGCCCCATGGTCCTTCAGA AAGAATTTCTCAAAAGAAGCCATGAACTCCACAGATTTGTACCCACTACTATGCCACCTCCTC AATATCACTGCCATGCCACAATGGATCATTCTGGAATGTCCAGGATCTGCTCAATTCAGCA ATGCCAAGGGTGGTCCCTTATACACAGAGTACTATACTCCTCCCTGGTAGTGTTAAACCAGCA GAATATGACCAAGAGGGGTCATACCCTTATTTCATAGGGGTCTCTCTTGGCAGCATTATAGTG ATTGTATTTTTTGTAATTTCATTAAGCATTTAATTCACAGTCAAATACCTGCCTTACAAGAT ATGCATGCTGAAATAGCTCAACCATTATTACAAGCC<u>TAA</u>TGTTACTTTGAAGTGGATTTGCAT ATTGAAGTGGAGATTCCATAATTATGTCAGTGTTTTAAAGGTTTTCAAATTCTGGGAAACCAGTT CACATACACACACAGGACCAAAATACTTACACCTGCAAAGGAATAAAGATGTGAGAGTATGT CTCCATTGTTCACTGTAGCATAGGGATAGATAAGATCCTGCTTTATTTGGACTTGGCCAGAT AATGTATATATTTAGCAACTTTGCACTATGTAAAGTACCTTATATATTGCACTTTAAATTTCT CTCCTGATGGGTACTTTAATTTGAAATGCACTTTATGGACAGTTATGTCTTATAACTTGATTG AAAATGACAACTTTTTGCACCCATGTCACAGAATACTTGTTACGCATTGTTCAAACTGAAGGA GGTGATAAGTGTTGAAAATTAAATGTGATAACCTTTGAACCTTGAATTTTGGAGATGTATTCC TTTATTTTCCCTCAAAAGAGAGTCAAATACTGACAGATTCGTTCTAAATATATTGTTTCTGT CATAAAATTATTGTGATTTCCTGATGAGTCATATTACTGTGATTTTCATAATAATGAAGACAC CATGAATATACTTTCTATATAGTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCAT

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FIGURE 452

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVKQ
VTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIWIT
NQRAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLYWED
PDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEERLIEL
DQYLDKDHYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYNSRIQP
IIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTDLYPLLC
HLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYFIGVSLGS
IIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

Important features:

Signal Peptide:

amino acids 1-22

Transmembrane Domain:

amino acids 429-452

N-glycosylation sites:

amino acids 101-104, 158-161, 292-295, 329-332, 362-365, 369-372, 382-385, 389-392

Somatomedin B Domain:

amino acids 69-85

Sulfatase protein Region:

amino acids 212-241

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FIGURE 453

GGCCGCCTGGAATTGTGGGAGTTGTCTGCCACTCGGCTGCCGGAGGCCGAAGGTCCGTGAC ${ t TATG}{ t GCTCCCCAGAGCCTGCCTTCATCTAGGATGCCTCCTCTGGGCATGCTGCTTGGGCTGCT}$ GATGGCCGCCTGCTTCACCTTCTGCCTCAGTCATCAGAACCTGAAGGAGTTTGCCCTGACCAA TGCCGAAGTCCTGGAGGTGTTCCACCCGACGCATGAGTGGCAGGCCCTTCAGCCAGGGCAGGC TGTCCCTGCAGGATCCCACGTACGGCTGAATCTTCAGACTGGGGAAAGAGAGGCCAAAACTCCA ATATGAGGACAAGTTCCGAAATAATTTGAAAGGCAAAAGGCTGGATATCAACACCAACACCTA CACATCTCAGGATCTCAAGAGTGCACTGGCAAAATTCAAGGAGGGGGCAGAGATGGAGAGTTC AAAGGAAGACAAGGCAAGGCAGGCTGAGGTAAAGCGGCTCTTCCGCCCCATTGAGGAACTGAA GAAAGACTTTGATGAGCTGAATGTTGTCATTGAGACTGACATGCAGATCATGGTACGGCTGAT CAACAAGTTCAATAGTTCCAGCTCCAGTTTGGAAGAGAAGATTGCTGCGCTCTTTGATCTTGA ATATTATGTCCATCAGATGGACAATGCGCAGGACCTGCTTTCCTTTGGTGGTCTTCAAGTGGT GATCAATGGGCTGAACAGCACAGAGCCCCTCGTGAAGGAGTATGCTGCGTTTGTGCTGGGCGC TGCCTTTTCCAGCAACCCCAAGGTCCAGGTGGAGGCCATCGAAGGGGGAGCCCTGCAGAAGCT GCTGGTCATCCTGGCCACGGAGCAGCCGCTCACTGCAAAGAAGAAGGTCCTGTTTGCACTGTG CTCCCTGCTGCGCCACTTCCCCTATGCCCAGCGGCAGTTCCTGAAGCTCGGGGGGCTGCAGGT CCTGAGGACCCTGGTGCAGGAGAAGGGCACGGAGGTGCTCGCCGTGCGCGTGGTCACACTGCT CTACGACCTGGTCACGGAGAAGATGTTCGCCGAGGAGGAGGCTGAGCTGACCCAGGAGATGTC CCCAGAGAAGCTGCAGCAGTATCGCCAGGTACACCTCCTGCCAGGCCTGTGGGAACAGGGCTG GTGCGAGATCACGGCCCACCTCCTGGCGCTGCCCGAGCATGATGCCCGTGAGAAGGTGCTGCA GACACTGGGCGTCCTCCTGACCACCTGCCGGGACCGCTACCGTCAGGACCCCCAGCTCGGCAG GACACTGGCCAGCCTGCAGGCTGAGTACCAGGTGCTGGCCAGCCTGGAGCTGCAGGATGGTGA GGACGAGGCTACTTCCAGGAGCTGCTGGGCTCTGTCAACAGCTTGCTGAAGGAGCTGAGA**TG A**GGCCCCACACCAGGACTGGACTGGGATGCCGCTAGTGAGGCTGAGGGGTGCCAGCGTGGGTG GGCTTCTCAGGCAGGAGGACATCTTGGCAGTGCTGGCCTTGGCCATTAAATGGAAACCTGAAGG

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FIGURE 454

MAPQSLPSSRMAPLGMLIGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEELD
AEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTNTY
TSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMVRLI
NKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEPLVKEYAAFVLGA
AFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKLGGLQV
LRTLVQEKGTEVLAVRVVTLLYDLVTEKMFAEEEAELTQEMSPEKLQQYRQVHLLPGLWEQGW
CEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLASLELQDGE
DEGYFQELLGSVNSLLKELR

Important features:

Signal peptide:

amino acids 1-29

Hypothetical YJL126w/YLR351c/yhcX family protein.

amino acids 364-373

N-glycosylation site.

amino acids 193-197, 236-240

N-myristoylation site.

amino acids 15-21, 19-25, 234-240, 251-257, 402-408, 451-457

Homologous region SLS1 protein.

amino acids 68-340

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FIGURE 455

GCCCCAGGGAGCAGTGGTTATAACTCAGGCCCGGTGCCCAGAGCCCAGGAGGAGGAGGCAGT GGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCCACCCCCTA CTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCTAGAC TCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCGTCCTTG TGGTTCCTCTCTCCTGGGGAAATAAGGTGCAGCGGCCATGGCTACAGCAAGACCCCCCTGGA TGTGGGTGCTCTGTCTCACAGCCTTGCTTCTGGGGGGTCACAGAGCATGTTCTCGCCA ACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCAGGACCTGG GAGCTGGGGCCGGGAAGACGCCCGGTCGGATGACAGCAGCCGCATCATCAATGGATCCG ACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAACCAGCTCTACT GCGGGGCGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCACTGCAGGAAGAAGTTT TCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGCAGCAGATGTTCC AGGGGGTCAAATCCATCCCCACCCTGGCTACTCCCACCCTGGCCACTCTAACGACCTCATGC TCATCAAACTGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCATCAACGTCTCCTCTC TGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGTCAGAAAAGGTGCGAGG ATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGACAAAGCAGGTAGAGACT CCTGCCAGGGTGATTCTGGGGGGGCCTGTGGTCTGCAATGGCTCCCTGCAGGGACTCGTGTCCT GGGGAGATTACCCTTGTGCCCGGCCCAACAGACCGGGTGTCTACACGAACCTCTGCAAGTTCA CCAAGTGGATCCAGGAAACCATCCAGGCCAACTCC**TGA**GTCATCCCAGGACTCAGCACACCGG TGTTGAGAATGTTCATCTCCAGCCCCTGACCCCATGTCTCCTGGACTCAGGGTCTGCTTCC CCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCTGGGAACAATTTCCAAAACTGTCCAG GGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTCATCCTCAAGCTCAGGGCCCATCCCTT

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FIGURE 456

MATARPPWMWVLCALITALLLGVTEHVLANNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDDS SSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLSPV YESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPSAGTKCLVSG WGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGRDSCQGDSGGPVVCN GSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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FIGURE 457

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCTTGCTTCCTGAACT AGCTCACAGTAGCCCGGCGGCCCAGGGCAATCCGACCACATTTCACTCTCACCGCTGTAGGAATCCAGATGCAGG CCAAGTACAGCACGAGGGACATGCTGGATGATGATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTG CCACAACTCGGCATCCAGAGCCCCGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGA $\tt CCCTGCTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTCAGTACTACCAGC$ TTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGCTGAAAAACTCTGTCGTGAGCTGTATAACA AAGCTGGAGCACACGGTGCAGCCCTTGTACAGAACAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATA AAGAAGACCTGGAATTTGCCGCGTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTTTGCGCC CTGACAGTGGCAAGGCCTGGCTGTGGATGGAACCCCTTTCACTTCTGAACTGTTCCATATTATAATAGATG TCACCAGCCCAAGAAGCAGACTGTGTGGCCATCCTCAATGGGATGATCTTCTCAAAGGACTGCAAAGAATTGA AGCGTTGTGTCTGTGAGAGGGCAGGAATGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCG AAGGTGAC<u>TGA</u>TTCGCCCTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAG ACATTGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTGTTTCCTGTT CAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACAAGAAGTCTTATTTACATGCCAC CAACCAACCTCAGAAACCCATAATGTCATCTGCCTTCTTGGCTTAGAGATAACTTTTAGCTCTCTTTCTCTCAA TGTCTAATATCACCTCCTGTTTTCATGTCTTCCTTACACTTGGTGGAATAAGAAACTTTTTGAAGTAGAGGAAA TACATTGAGGTAACATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTAC CAGCAAATACACAAGGAATTCTTTTTGTTTGTTTCAGTTCATACTAGTCCCTTCCCAATCCATCAGTAAAGACCC CATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAGAATCTCAAATCTCAATGCCTTATAA ATCCCCATCTCCGTTTCATATCAGAACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAAGT GAGCCTCTTCATCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAGGT ACTGAAGATTTAATAATAATAATGTAAATACTGTGAAAAA

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FIGURE 458

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLLI GLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRELY NKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAASQSY SEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKDCKEL KRCVCERRAGMVKPESLHVPPETLGEGD

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FIGURE 459

GTTGATGGCAAACTTCCTCAAAGGAGGGGCAGAGCCTGCGCAGGGCAGGAGCAGCTGGCCCAC TGGCGGCCCGCAACACTCCGTCTCACCCTCTGGGCCCACTGCATCTAGAGGAGGGCCGTCTGT GAGGCCACTACCCCTCCAGCAACTGGGAGGTGGGACTGTCAGAAGCTGGCCCAGGGTGGTGGT CAGCTGGGTCAGGGACCTACGGCACCTGCTGGACCACCTCGCCTTCTCCATCGAAGCAGGGAA GTGGGAGCCTCGAGCCCTCGGGTGGAAGCTGACCCCAAGCCACCCTTCACCTGGACAGGATGA GAGTGTCAGGTGTGCCTTCGCCTCCTGGCCCTCATCTTTGCCATAGTCACGACATGGATGTTTA CCACCAAGGAGATCCAGGTTAAAAAGTACAAGTGTGGCCTCATCAAGCCCTGCCCAGCCAACT ACTTTGCGTTTAAAATCTGCAGTGGGGCCGCCAACGTCGTGGGCCCTACTATGTGCTTTGAAG ACCGCATGATCATGAGTCCTGTGAAAAACAATGTGGGCAGAGGCCTAAACATCGCCCTGGTGA ATGGAACCACGGGAGCTGTGCTGGGACAGAAGGCATTTGACATGTACTCTGGAGATGTTATGC ACCTAGTGAAATTCCTTAAAGAAATTCCGGGGGGGTGCACTGGTGCTGGTGGCCTCCTACGACG ATCCAGGGACCAAAATGAACGATGAAAGCAGGAAACTCTTCTCTGACTTGGGGAGTTCCTACG CAAAACAACTGGGCTTCCGGGACAGCTGGGTCTTCATAGGAGCCAAAGACCTCAGGGGTAAAA TGCTGGAGATGGAGGGCTGCATGCCCCCGAAGCCATTTTAGGGTGGCTGTGGCTCTTCCTCAG CCAGGGGCCTGAAGAAGCTCCTGCCTGACTTAGGAGTCAGAGCCCGGCAGGGGCTGAGGAGGA GGAGCAGGGGGTGCTGCGTGGAAGGTGCTGCAGGTCCTTGCACGCTGTGTCGCGCCTCTCCTC CTCGGAAACAGAACCCTCCCACAGCACATCCTACCCGGAAGACCAGCCTCAGAGGGTCCTTCT GGAACCAGCTGTCTGTGGAGAGAATGGGGTGCTTTCGTCAGGGACTGCTGACGGCTGGTCCTG AGGAAGGACAAACTGCCCAGACTTGAGCCCAATTAAATTTTATTTTTTGCTGGTTTTTGAAAAAAA AAAAAAAAAAA

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FIGURE 460

MRVSGVLRLLALIFAIVTTWMFIRSYMSFSMKTIRLPRWLAASPTKEIQVKKYKCGLIKPCPA NYFAFKICSGAANVVGPTMCFEDRMIMSPVKNNVGRGLNIALVNGTTGAVLGQKAFDMYSGDV MHLVKFLKEIPGGALVLVASYDDPGTKMNDESRKLFSDLGSSYAKQLGFRDSWVFIGAKDLRG KSPFEQFLKNSPDTNKYEGWPELLEMEGCMPPKPF

Important features:

Signal peptide:

amino acids 1-15

ATP/GTP-binding site motif A (P-loop).

amino acids 184-191

N-glycosylation site.

amino acids 107-110

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FIGURE 461

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGGA AACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCCTC TAGAACCCGACCCACCACCATGAGGTCCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGGCGT CCAGTGGTCCTTGCTTCTGGCTGTCCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTATTAA GTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGACAACCATCTATGCAGA GCCAGCGCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCAAGGCCCACACCACCGGAGA GAGGGCAGCATGGAAGAGCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTCACCCAGAGG GCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCCAGGACACAAA GACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACGGTGTCAGAGAA GCACCAGGGCAAAGCGCCAACCACAGCCAAGACGCTCATTCCCAAAAGTCAGCACAGAATGCT GGCTCCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCACAGCAGTCATCCC ACCTAAGGAGAAGAACCTCAGGCCACCCCACCCCTGCCCCTTTCCAGAGCCCCACGACGCA GAGAAACCAAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTGGGATTTTGAGGAAAA ATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTGTGAAGATCAAAGCCTC CAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTCTTCCTGGACTCCAGACA CTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACCCTTTGGCTTCATGGAGCT CAACTACTCCTTGGTGCAGAAGGTCGTGACACGCTTCCCTCCAGTGCCCCAGCAGCAGCTGCT CCTGGCCAGCCTCCCGCTGGGAGCCTCCGGTGCATCACCTGTGCCGTGGTGGGCAACGGGGG CATCCTGAACAACTCCCACATGGGCCAGGAGATAGACAGTCACGACTACGTGTTCCGATTGAG CGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGGACTCGGACATCCTTCTACGGCTTTAC CGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAATCGGGGTTTCAAGAACGTGCCTCT TGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCACCCGGGACTATGAGTGGCTGGAAGC ACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTTTCTGGTTCAGGCACAGACCCCAGGA AGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTGTTGCTGCACCCAGACTTTCTCCGATA CATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGATGGTGCCCACTGGAGGATATACCGCCC CACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTCAGCTCTGTGACCAGGTGAGTGCTTATGG CTTCATCACTGAGGGCCATGAGCGCTTTTCTGATCACTACTATGATACATCATGGAAGCGGCT AGGGATAATCCGGCTGTACCAGCGTCCTGGTCCCGGAACTGCCAAAGCCAAGAAC**TGA**CCGGG GCCAGGGCTGCCATGGTCTCCTTGCCTGCTCCAAGGCACAGGATACAGTGGGAATCTTGAGAC TCTTTGGCCATTTCCCATGGCTCAGACTAAGCTCCAAGCCCTTCAGGAGTTCCAAGGGAACAC TTGAACCATGGACAAGACTCTCTCAAGATGGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCA CCACAATTCCTGCTGAAAAACACTCTTCCAGTCCAAAAGCTTCTTGATACAGAAAAAAAGAGCC TGGATTTACAGAAACATATAGATCTGGTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCT TGAAGGTATTACTTAACTTCACTACAGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTC TAGAAGGGTCTATACTTGTCCTTGTCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAAC AAAAAAA

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FIGURE 462

MRSCLWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKPK
SQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAWKS
PEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQGKAA
TTAKTLIPKSQHRMLAPTGAVSTRTRQKGVTTAVIPPKEKKPQATPPPAPFQSPTTQRNQRLK
AANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHFNQSEW
DRLEHFAPPFGFMELNYSLVQKVVTRFPPVPQQQLLLASLPAGSLRCITCAVVGNGGILNNSH
MGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGFTAFSLTQSLLILGNRGFKNVPLGKDVRY
LHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFLRYMKNRFL
RSKTLDGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYYDTSWKRLIFYINH
DFKLEREVWKRLHDEGIIRLYQRPGPGTAKAKN

Important features:

Cytoplasmic Domain:

amino acids 1-10

Type II Transmembrane Domain:

amino acids 11-35

Lumenal catalytic Domain:

amino acids 36-600

Ribonucleotide Reductase small subunit Signature:

amino acids 481-496

N-glycosylation Sites:

amino acids 300-303, 311-314, 331-334, 375-378, 460-463

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FIGURE 463

GGGGGAGCTAGGCCGGCGGCAGTGGTGGTGGCGGCGCGCCAAGGGTGAGGGCGGCCCCAGAAC CCCAGGTAGGCCGCCGCAGTGGTGGTGGCGCCCCAAATGGTCAGGCCCCCAAATGCCCCCCAAATGCCCCCCCAACTGTC
ATTTCTACTTTCCTCACTGTTGGCTCTCTTAACTGTGTCCACTCCTTCATGGTGTCAGAGCAC
TGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCTTGGAATAAAATACGACTTCCTGA
GTACGTCATCCAGCAAACTAGATCTCTTGATCCATGCAAACCTTACCACGCTGACCTTCTG
GGGAACCACGAAAGTAGAAATCACACGCCAGCACCACCACCACCATCATCCTGCATAGTCA
CCCCCTGCAGATATCTAGGGCCACCCTCAGGAAGGCTGGAGGAGGAGGCTATCCGAAGAACC GACTCTTCTAGAATTTTATGAGGATTATTTCAGCATACCGTATCCCCTACCCAAACAAGATCT TGCTGCTATTCCCGACTTTCAGTCTGGTGCTATGGAAAACTGGGGACTGACAACATATAGAGA ATCTGCTCTGTTGTTTGATGCAGAAAAGTCTTCTGCATCAAGTAAGCTTGGCATCACAGTGAC TGTGGCCCATGAACTGGCCCACCAGTGGTTTGGGAACCTGGTCACTATGGAATGGTGGAATGA CTCTTTGAAAGAAATGGTTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTGAAGA AAACATCGGTTGGATGGATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAAGCT ${\tt TGAACGTATG} \underline{{\tt TAA}}{\tt AAATTCCTCCCTTGCCCGGTTCCTGTTATCTCTAATCACCAACATTTTGTTGGGTGTATTTTCAAACTAGAGATGGCTGTTTTTGGCTCCAACTGGAGATACTTTTTTCCCTTC}$ AACTCATTTTTTGACTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTCATGAATGGGCTTTTT CATGAATGGGCTATCGCTACCATGTGTTTTTGTTCATCACAGGTGTTGCCCTGCAACGTAAACC AAAAAAAAAA

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FIGURE 464

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVHY
DLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLEHP
PQEQIALLAPEPLLVGLPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTAARM
AFPCFDEPAFKASFSIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVAFIIS
DFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLEFYEDYFSIPYPLPKQDLAAIPDFQ
SGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDLWLNEGF
AKFMEFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFDDVSYDKG
ACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDGFCSRSQHS
SSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPDTGYLWHVPL
TFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSLTGLLKGTHTA
VSSNDRASLINNAFQLVSIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIPMYKLMEKRDMN
EVETQFKAFLIRLLRDLIDKQTWTDEGSVSEQMLRSELLLLACVHNYQPCVQRAEGYFRKWKE
SNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALCRTQNKEKLQWLLD
ESFKGDKIKTQEFPQILTLIGRNPVGYPLAWQFLRKNWNKLVQKFELGSSSIAHMVMGTTNQF
STRTRLEEVKGFFSSLKENGSQLRCVQQTIETIEENIGWMDKNFDKIRVWLQSEKLERM

Important features:

Signal peptide:

amino acids 1-34

N-glycosylation sites:

amino acids 70-74, 154-158, 414-418, 760-764, 901-905

Neutral zinc metallopeptidases, zinc-binding region signature:

amino acids 350-360

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FIGURE 465

 ${\tt CAGCCACAGACGGGTC{\color{red} {\bf ATG}} {\tt AGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCACT}}$ GCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCCGA CCTACCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGACAC GTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGGAGGC CAAGGACCAGGAGCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATCTCCTA CCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCCAGTCTGCTTGTCTATGGAAGGCTG TCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACTGTTATGATGGCCTCCT TTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCGTGGGTATGACTGAGAACTGCAATAG GAAAGATTTTCTGACCTGTCATCGGGGGACCACCATTATGACACGGGAAACTTGGCTCAAGA ACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGTGTGTCAGGAGAC GCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAGGCTGCAGCACTGT TGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCTCCTGGGGTGCTTGTGGCCTC CTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAGCAGCGTTCTGCTGAA CTCCCTCCTCAAGCTGCCCCTGTCCCAGGAGACCGGCAGTGTCCTACCTGTGTGCAGCC CCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGGGGCCCCCCACTCATTGTTA TGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAATGAGCATTCAGGGCTGCGT GGCCCAACCTTCCAGCTTCTTGTTGAACCACACCAGACAAATCGGGATCTTCTCTGCGCGTGA TCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTGGTGGGGGAGTGGTTTGCCCTTC TGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTCCCATTCTGTCCATGAATCATCTT CCCCACACACATCATTCATATCTACTCACCTAACAGCAACACTGGGGAGAGCCTGGAGCATC CGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTGGCTGCATGTATCTGATAATACAGAC CCTGTCCTTTCA

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FIGURE 466

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLIE SGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQPPA DPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRLRGGGIFSNLRVQGCMPQPGCNLLN GTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETLLLID VGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLNSLPPQ AAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGCVAQPSS FLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVCPSC

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FIGURE 467

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGCACCACCGGAGCCCTTGAGACATCCTTG AGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTTTTTGCAGG**ATG**ATGGTGGCCCTTCG AGGAGCTTCTGCATTGCTGGTTCTGTTCCTTGCAGCTTTTCTGCCCCCGCCGCAGTGTACCCA GGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGGAAAA ATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTTCTCAAAAAAATATATCTGT CATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGCAGTGGGTAACTTGGCACT CATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAAGAAGAAAAA GATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTCTTTGAAAAT AGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATAACTCTCCAAA GGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAACATACGGGCATT CATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTCCTGGCAGGGAAC AGGCCAAGTGATCTACAAAGGTTTTCTATTTTTTCATAACCAAGCAACTTCTAATGAGATAAT CAAATATAACCTGCAGAAGAGGACTGTGGAAGATCGAATGCTGCTCCCAGGAGGGGTAGGCCG AGCATTGGTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGTGGATGAGCATGGGCT CTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCACAAAGATTGAGCCGGG CACACTGGGAGTGGAGCATTCATGGGATACCCCATGCAGAAGCCAGGATGCTGAAGCCTCATT CCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCCAGGGCCCTCATCGCATCAC CTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGCCCCAACTTGTTCTTCCCCAA GAGACCAAGAAGTCACTCCATGATCCATTACAACCCCAGAGATAAGCAGCTCTATGCCTGGAA TGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAAGCTGCCTCTGAAG**TAA**TGCAT TACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTCTACAGGACAGTGAGGCTATAGC CCCTTCACAATATAGTATCCCTCTAATCACACAGGAAGAGTGTGTAGAAGTGGAAATACGT ATGCCTCCTTTCCCAAATGTCACTGCCTTAGGTATCTTCCAAGAGCTTAGATGAGAGCATATC ATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAAACCTCCTGGCTCTCAAGGATGACCAC ATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACTGCTCCCCAGCATTTACTGTAACTCTG CCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGCCCCTAATATTCACCACTGGCTTTTCTC TCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTTCAAATGTCTATTGATATTCTCCCATTTT CTCACTATGTTGCCCAGGCTGGTCTCAAACTCCAGAGCTCAAGAGATCCTCCTGCCTCAGCCT CCTAAGTACCTGGGATTACAGGCATGTGCCACCACACCTGGCTTAAAATACTATTTCTTATTG AGGTTTAACCTCTATTTCCCCTAGCCCTGTCCTTCCACTAAGCTTGGTAGATGTAATAATAAA GTGAAAATATTAACATTTGAATATCGCTTTCCAGGTGTGGAGTGTTTGCACATCATTGAATTC TCGTTTCACCTTTGTGAAACATGCACAAGTCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGT AACACAATTACAAAGTGAAAGATACAGCTAGAAAATACTACAAATCCCATAGTTTTTCCATTG CCCAAGGAAGCATCAAATACGTATGTTTGTTCACCTACTCTTATAGTCAATGCGTTCATCGTT TCAGCCTAAAAATAATAGTCTGTCCCTTTAGCCAGTTTTCATGTCTGCACAAGACCTTTCAAT AGGCCTTTCAAATGATAATTCCTCCAGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCC TCCTCTTGTCTTGCTCTCTGTTTCTCTCTTTTCTGCTTTAAATTCAATAAAAGTGACACTG AGCAAAAAAAAAAAAA

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FIGURE 468

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFRVLEQGLEKCTQATRAYIQEFQEF SKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLLQE AEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNSPKVYLLIGSRNNTVWEF ANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVEDRMLL PGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKIEPGTLGVEHSWDTPCRSQ DAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIHYNPRDK QLYAWNEGNQIIYKLQTKRKLPLK

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FIGURE 469

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGGC AGTGTTTTGCCTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCCTC CTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGTGGG GCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCTGGGG CGGGAAGGCGAGGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCAAGCAC CACACCTGTCCTTGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTACCGCTGC TCCATGGACTTGAAGAACATCAATTTT**TAG**GCGCTTGCCTGGTCTCAGGATACCCACCATCCT TTTCCTGAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGACTCTCCCAG TCCCTACACTGACTACCCTGATCTCTCTTGTCTAGTACGCACATATGCACACAGGCAGACATA CCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGGCTGTGGTGTG AAAGGTGGCCAGCCTGGTTCTCTCCCTGCTCAGGCTGCCAGAGAGGTGGTAAATGGCAGAAA GGACATTCCCCCTCCCCCAGGTGACCTGCTCTTTTCCTGGGCCCTGCCCCTCTCCCCA CATGTATCCCTCGGTCTGAATTAGACATTCCTGGGCACAGGCTCTTGGGTGCATTGCTCAGAG TCCCAGGTCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGGACCAATTTGTGGGT AGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGACTCAAGATTGGCTCTT CCCAGAGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCAGGGAGGCCAATCAGCC CCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGACCTGTGACCTTCTGCCA GAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGTTAACCACTGAAGCCCCCA ATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAATCTAATCTGATATTGACAT ATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACTCCTTTCCAAGGATCAGCCCTGAGAGCAG GTTGGTGACTTTGAGGAGGCAGTCCTCTGTCCAGATTGGGGTGGGAGCAAGGGACAGGGAGC AGGGCAGGGGCTGAAAGGGGCACTGATTCAGACCAGGGAGGCAACTACACACCAACATGCTGG CTTTAGAATAAAAGCACCAACTGAAAAAA

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FIGURE 470

MRGATRVSIMLLLVTYSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHPG SHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

Important feratures:

Signal peptide:

amino acids 1-19

Tyrosine kinase phosphorylation site:

amino acids 88-95

N-myristoylation sites:

amino acids 33-39, 35-41, 46-52

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FIGURE 471

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCTTTCC TCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGCTG CTGCCTTGGCATTGCTGCTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGGCCC TGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAAGCAA AGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTTCCTCT GTCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCGTCCCCC TCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTATTTCAAAG GAGAAATCTTCCTGGATGAAAAGAAAAGTTCTATGGTCCACAAAGGCGGAAGATGATGTTTA TGGGATTTATCCGTCTGGGAGTGTGGTACAACTTCTTCCGAGCCTGGAACGGAGGCTTCTCTG GAAACCTGGAAGGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCAGGAAAGCAGG GCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACTTTCTGTTCTGG AAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAA<mark>TGA</mark>TTGTGTGAAACTG CCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTCATGGGATGTATTGTTTCCACTCGTG TCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTATTAATGTATTTAA TATTCTGTTTAGGCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGACAAAAATCTGAAAAA CTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAATTGACTGCCAGGCTGG GTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGGTGAGCAAGTCACTTGAG GTCGGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTCTCTACTAAAAATACAAAA ATCACCCGGGTGTGGCAGCACCTGTAGTCCCAGCTACCCGGGAGGCTGAGGCAGGAGAA ${\tt TCACTTGAACCTGGGAGGTTGCGGTGAGCTGAGATCACACCACTGTATTCCAGCCTG}$ GGTGACTGAGACTCTAACTAA

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FIGURE 472

MSFLQDPSFFTMGMWSIGAGALGAAALALLLANTDVFLSKPQKAALEYLEDIDLKTLEKEPRT FKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDFQP YFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEGFILGGVFVVGS GKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

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FIGURE 473

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FIGURE 474

MTFFLSLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGKG IVKGRNLDSRGLILGAEAWGRGVKKNT

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FIGURE 475

GACAGTGGAGGGCAGTGGAGAGGACCGCGCTGTCCTGCTGTCACCAAGAGCTGGAGACACCAT CTCCCACCGAGAGTC**ATG**GCCCCATTGGCCCTGCACCTCCTCGTCCTCGTCCCCATCCTCCTC AGCCTGGTGGCCTCCCAGGACTGGAAGGCTGAACGCCAGGCCAAGACCCCTTCGAGAAATGCATG CAGGATCCTGACTATGAGCAGCTGCTCAAGGTGGTGACCTGGGGGGCTCAATCGGACCCTGAAG CCCCAGAGGGTGATTGTGGTTGGCGCTGGTGGCCGGGCTGGTGGCCGCCAAGGTGCTCAGC GATGCTGGACACAAGGTCACCATCCTGGAGGCAGATAACAGGATCGGGGGCCGCATCTTCACC TACCGGGACCAGAACACGGGCTGGATTGGGGAGCTGGGAGCCATGCGCATGCCCAGCTCTCAC AGGATCCTCCACAAGCTCTGCCAGGGCCTGGGGCTCAACCTGACCAAGTTCACCCAGTACGAC AAGAACACGTGGACGGAGGTGCACGAAGTGAAGCTGCGCAACTATGTGGTGGAGAAGGTGCCC GAGAAGCTGGGCTACGCCTTGCGTCCCCAGGAAAAGGGCCACTCGCCCGAAGACATCTACCAG ATGGCTCTCAACCAGGCCCTCAAAGACCTCAAGGCACTGGGCTGCAGAAAGGCGATGAAGAAG CAGCTTCTGGGAGACGTGATGTCCGAGGATGGCTTCTTCTATCTCAGCTTCGCCGAGGCCCTC CTGCCGCGCGCTGCTGAGCTCGCTGTCCGGGCTTGTGCTGTTGAACGCGCCCGTGGTGGCG ATGACCCAGGGACCGCACGATGTGCACGTGCAGATCGAGACCTCTCCCCCGGCGCGGAATCTG AAGGTGCTGAAGGCCGACGTGGTGCTGACGGCGAGCGGACCGGCGGTGAAGCGCATCACC TTCTCGCCGCCGCCGCCACATGCAGGAGGCGCTGCGGAGGCTGCACTACGTGCCGGCC ACCAAGGTGTTCCTAAGCTTCCGCAGGCCCTTCTGGCGCGAGGAGCACATTGAAGGCGGCCAC TCAAACACCGATCGCCCGTCGCGCATGATTTTCTACCCGCCGCCGCGCGAGGGCGCGCTGCTG CTGGCCTCGTACACGTGGTCGGACGCGGCGGCAGCGTTCGCCGGCTTGAGCCGGGAAGAGGCG TTGCGCTTGGCGCTCGACGACGTGGCGGCATTGCACGGGCCTGTCGTGCGCCAGCTCTGGGAC GGCACCGGCGTCGTCAAGCGTTGGGCGGAGGACCAGCAAGCCAGGGTGGCTTTGTGGTACAG CCGCCGGCGCTCTGGCAAACCGAAAAGGATGACTGGACGGTCCCTTATGGCCGCATCTACTTT GCCGGCGAGCACCGCCTACCCGCACGGCTGGGTGGAGACGGCGGTCAAGTCGGCGCTGCGC GCCGCCATCAAGATCAACAGCCGGAAGGGGCCTGCATCGGACACGGCCAGCCCCGAGGGGCAC GCATCTGACATGGAGGGGCAGGGGCATGTGCATGGGGTGGCCAGCAGCCCCTCGCATGACCTG GCAAAGGAAGAAGCCACCCTCCAGTCCAAGGCCAGTTATCTCTCCAAAACACGACCCAC AAAAAAAAAAAAA

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FIGURE 476

MAPLALHLLVLVPILLSLVASQDWKAERSQDPFEKCMQDPDYEQLLKVVTWGLNRTLKPQRVI
VVGAGVAGLVAAKVLSDAGHKVTILEADNRIGGRIFTYRDQNTGWIGELGAMRMPSSHRILHK
LCQGLGLNLTKFTQYDKNTWTEVHEVKLRNYVVEKVPEKLGYALRPQEKGHSPEDIYQMALNQ
ALKDLKALGCRKAMKKFERHTLLEYLLGEGNLSRPAVQLLGDVMSEDGFFYLSFAEALRAHSC
LSDRLQYSRIVGGWDLLPRALLSSLSGLVLLNAPVVAMTQGPHDVHVQIETSPPARNLKVLKA
DVVLLTASGPAVKRITFSPPLPRHMQEALRRLHYVPATKVFLSFRRPFWREEHIEGGHSNTDR
PSRMIFYPPPREGALLLASYTWSDAAAAFAGLSREEALRLALDDVAALHGPVVRQLWDGTGVV
KRWAEDQHSQGGFVVQPPALWQTEKDDWTVPYGRIYFAGEHTAYPHGWVETAVKSALRAAIKI
NSRKGPASDTASPEGHASDMEGQGHVHGVASSPSHDLAKEEGSHPPVQGQLSLQNTTHTRTSH

Important features:

Signal peptide:

amino acids 1-21

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FIGURE 477

GAACTCAGAGCCGGGAAGCCCCCATTCACTAGAAGCACTGAGAGATGCGGCCCCCTCGCAGGGTCTGAATTTCCT GCTGCTGTTCACAAAGATGCTTTTTATCTTTAACTTTTTGTTTTCCCCACTTCCGACCCCGGCGTTGATCTGCAT CCTGACATTTGGAGCTGCCATCTTCTTGTGGCTGATCACCAGACCTCAACCCGTCTTACCTCTTCTTGACCTGAA CAATCAGTCTGTGGGAATTGAGGGAGGAGCACGGAAGGGGGTTTCCCAGAAGAACAATGACCTAACAAGTTGCTG CTTCTCAGATGCCAAGACTATGTATGAGGTTTTCCAAAGAGGACTCGCTGTGTCTGACAATGGGCCCTGCTTGGG ATATAGAAAACCAAACCAGCCCTACAGATGGCTATCTTACAAACAGGTGTCTGATAGAGCAGAGTACCTGGGTTC CTGTCTCTTGCATAAAGGTTATAAATCATCACCAGACCAGTTTGTCGGCATCTTTGCTCAGAATAGGCCAGAGTG GATCATCTCCGAATTGGCTTGTTACACGTACTCTATGGTAGCTGTACCTCTGTATGACACCTTGGGACCAGAAGC CATCGTACATATTGTCAACAAGGCTGATATCGCCATGGTGATCTGTGACACACCCCAAAAGGCATTGGTGCTGAT AGGGAATGTAGAGAAAGGCTTCACCCCGAGCCTGAAGGTGATCATCCTTATGGACCCCTTTGATGATGACCTGAA GCAAAGAGGGGAGAAGAGTGGAATTGAGATCTTATCCCTATATGATGCTGAGAACCTAGGCAAAGAGCACTTCAG AAAACCTGTGCCTCCTAGCCCAGAAGACCTGAGCGTCATCTGCTTCACCAGTGGGACCACAGGTGACCCCAAAGG AGCCATGATAACCCATCAAAATATTGTTTCAAATGCTGCTGCCTTTCTCAAATGTGTGGAGCATGCTTATGAGCC CACTCCTGATGATGTGGCCATATCCTACCTCCCTCTGGCTCATATGTTTGAGAGGATTGTACAGGCTGTTGTGTA CACATTGTTTCCCGCGGTGCCTCGACTCCTTAACAGGATCTACGATAAGGTACAAAATGAGGCCAAGACACCCTT GAAGAAGTTCTTGTTGAAGCTGGCTGTTTCCAGTAAATTCAAAGAGCTTCAAAAGGGTATCATCAGGCATGATAG TTTCTGGGACAAGCTCATCTTTGCAAAGATCCAGGACAGCCTGGGCGGAAGGGTTCGTGTAATTGTCACTGGAGC TGCCCCCATGTCCACTTCAGTCATGACATTCTTCCGGGCAGCAATGGGATGTCAGGTGTATGAAGCTTATGGTCA AACAGAATGCACAGGTGGCTGTACATTTACATTACCTGGGGACTGGACATCAGGTCACGTTGGGGTGCCCCTGGC TTGCAATTACGTGAAGCTGGAAGATGTGGCTGACATGAACTACTTTACAGTGAATAATGAAGGAGAGGTCTGCAT CAAGGGTACAAACGTGTTCAAAGGATACCTGAAGGACCCTGAGAAGACACAGGAAGCCCTGGACAGTGATGGCTG GCTTCACACAGGAGACATTGGTCGCTGGCTCCCGAATGGAACTCTGAAGATCATCGACCGTAAAAAGAACATTTT CAAGCTGGCCCAAGGAGAATACATTGCACCAGAGAAGATAGAAAATATCTACAACAGGAGTCAACCAGTGTTACA AATTTTTGTACACGGGGAGAGCTTACGGTCATCCTTAGTAGGAGTGGTGGTTCCTGACACAGATGTACTTCCCTC ATTTGCAGCCAAGCTTGGGGTGAAGGGCTCCTTTGAGGAACTGTGCCAAAACCAAGTTGTAAGGGAAGCCATTTT AGAAGACTTGCAGAAAATTGGGAAAGAAGTGGCCTTAAAACTTTTGAACAGGTCAAAGCCATTTTTCTTCATCC AGAGCCATTTTCCATTGAAAATGGGCTCTTGACACCAACATTGAAAGCAAAGCGAGGAGAGCTTTCCAAATACTT ${\tt TCGGACCCAAATTGACAGCCTGTATGAGCACATCCAGGAT} {\tt TAG}{\tt GATAAGGTACTTAAGTACCTGCCGGCCCACTG}$ ATCCTGTCTTTCCCATCTTCGATGTTGCTAATATTAAGGCTTCAGGGCTACTTTTATCAACATGCCTGTCTTCAA GATCCCAGTTTATGTTCTGTGTCCTCATGATTTCCAACCTTAATACTATTAGTAACCACAAGTTCAAGGGT ${\tt CAAAGGGACCCTCTGTGCCTTCTTTGTTTTTGTGATAAACATAACTTGCCAACAGTCTCTATGCTTATTTACA}$ TCTTCTACTGTTCAAACTAAGAGATTTTTAAATTCTGAAAAACTGCTTACAATTCATGTTTTCTAGCCACTCCAC AAACCACTAAAATTTTAGTTTTAGCCTATCACTCATGTCAATCATATCTATGAGACAAATGTCTCCGATGCTCTT $\tt CTGCGTAAATTAAATTGTGTACTGAAGGGAAAAGTTTGATCATACCAAACATTTCCTAAACTCTCTAGTTAGATA$ TCTGACTTGGGAGTATTAAAAATTGGGTCTATGACATACTGTCCAAAAGGAATGCTGTTCTTAAAGCATTATTTA CAGTAGGAACTGGGGAGTAAATCTGTTCCCTACAGTTTGCTGCTGAGCTGGAAGCTGTGGGGGAAGGAGTTGACA GGTGGGCCCAGTGAACTTTTCCAGTAAATGAAGCAAGCACTGAATAAAAACCTCCTGAACTGGGAACAAAGATCT ACAGGCAAGCAAGATGCCCACACAACAGGCTTATTTTCTGTGAAGGAACCAACTGATCTCCCCCACCCTTGGATT AGAGTTCCTGCTCTACCTTACCCACAGATAACACATGTTGTTTCTACTTGTAAATGTAAAGTCTTTAAAATAAAC TATTACAGATAAAAA

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FIGURE 478

MDALKPPCLWRNHERGKKDRDSCGRKNSEPGSPHSLEALRDAAPSQGLNFLLLFTKMLFIFNF
LFSPLPTPALICILTFGAAIFLWLITRPQPVLPLLDLNNQSVGIEGGARKGVSQKNNDLTSCC
FSDAKTMYEVFQRGLAVSDNGPCLGYRKPNQPYRWLSYKQVSDRAEYLGSCLLHKGYKSSPDQ
FVGIFAQNRPEWIISELACYTYSMVAVPLYDTLGPEAIVHIVNKADIAMVICDTPQKALVLIG
NVEKGFTPSLKVIILMDPFDDDLKQRGEKSGIEILSLYDAENLGKEHFRKPVPPSPEDLSVIC
FTSGTTGDPKGAMITHQNIVSNAAAFLKCVEHAYEPTPDDVAISYLPLAHMFERIVQAVVYSC
GARVGFFQGDIRLLADDMKTLKPTLFPAVPRLLNRIYDKVQNEAKTPLKKFLLKLAVSSKFKE
LQKGIIRHDSFWDKLIFAKIQDSLGGRVRVIVTGAAPMSTSVMTFFRAAMGCQVYEAYGQTEC
TGGCTFTLPGDWTSGHVGVPLACNYVKLEDVADMNYFTVNNEGEVCIKGTNVFKGYLKDPEKT
QEALDSDGWLHTGDIGRWLPNGTLKIIDRKKNIFKLAQGEYIAPEKIENIYNRSQPVLQIFVH
GESLRSSLVGVVVPDTDVLPSFAAKLGVKGSFEELCQNQVVREAILEDLQKIGKESGLKTFEQ
VKAIFLHPEPFSIENGLLTPTLKAKRGELSKYFRTQIDSLYEHIQD

Important features:

Type II transmembrane domain:

amino acids 61-80

Putative AMP-binding domain signature.

amino acids 314-325

N-glycosylation site.

amino acids 102-105, 588-591 and 619-622

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FIGURE 479

GGAGGCGGAGCCGCGGGCCGAGCAGTGAGGGCCCTAGCGGGGCCCGAGCGGGC CCGGGGCCCTAAGCCATTCCTGAAGTCATGGGCTGGCCAGGACATTGGTGACCCGCCAATCC . GGT**ATG**GACGACTGGAAGCCCAGCCCCTCATCAAGCCCTTTGGGGCTCGGAAGAAGCGGAGC TGGTACCTTACCTGGAAGTATAAACTGACAAACCAGCGGGCCCTGCGGAGATTCTGTCAGACA GGGGCCGTGCTTTTCCTGCTGGTGACTGTCATTGTCAATATCAAGTTGATCCTGGACACTCGG CGAGCCATCAGTGAAGCCAATGAAGACCCAGAGCCAGAGCAAGACTATGATGAGGCCCTAGGC CGCCTGGAGCCCCACGGCGCAGAGGCAGTGGTCCCCGGCGGGTCCTGGACGTAGAGGTGTAT TCAAGTCGCAGCAAAGTATATGTGGCAGTGGATGGCACCACGGTGCTGGAGGATGAGGCCCGG GAGCAGGGCCGGGGCATCCATGTCATTGTCCTCAACCAGGCCACGGGCCACGTGATGGCAAAA CGTGTGTTTGACACGTACTCACCTCATGAGGATGAGGCCATGGTGCTATTCCTCAACATGGTA GCGCCCGGCCGAGTGCTCATCTGCACTGTCAAGGATGAGGGCTCCTTCCACCTCAAGGACACA GCCAAGGCTCTGCTGAGGAGCCTGGGCAGCCAGGCTGGCCCTGCCCTGGGCTGGAGGGACACA TGGGCCTTCGTGGGACGAAAAGGAGGTCCTGTCTTCGGGGAAAACATTCTAAGTCACCTGCC CTCTCTTCCTGGGGGGACCCAGTCCTGCTGAAGACAGATGTGCCATTGAGCTCAGCAGAAGAG GCAGAGTGCCACTGGGCAGACACAGAGCTGAACCGTCGCCGGCGGCGCTTCTGCAGCAAAGTT GAGGGCTATGGAAGTGTATGCAGCTGCAAGGACCCCACACCCATCGAGTTCAGCCCTGACCCA CTCCCAGACAACAAGGTCCTCAATGTGCCTGTGGCTGTCATTGCAGGGAACCGACCCAATTAC CTGTACAGGATGCTGCGCTCTCTGCTTTCAGCCCAGGGGGTGTCTCCTCAGATGATAACAGTT TTCATTGACGGCTACTATGAGGAACCCATGGATGTGGTGGCACTGTTTGGTCTGAGGGGCATC CAGCATACTCCCATCAGCATCAAGAATGCCCGCGTGTCTCAGCACTACAAGGCCAGCCTCACT GCCACTTTCAACCTGTTTCCGGAGGCCAAGTTTGCTGTGGTTCTGGAAGAGGACCTGGACATT GCTGTGGATTTTTCAGTTTCCTGAGCCAATCCATCCACCTACTGGAGGAGGATGACAGCCTG TACTGCATCTCTGCCTGGAATGACCAGGGGTATGAACACACGGCTGAGGACCCAGCACTACTG TACCGTGTGGAGACCATGCCTGGGCTGGGTGCTCAGGAGGTCCTTGTACAAGGAGGAG CTTGAGCCCAAGTGGCCTACACCGGAAAAGCTCTGGGATTGGGACATGTGGATGCGGATGCCT GAACAACGCCGGGGCCGAGAGTGCATCATCCCTGACGTTTCCCGATCCTACCACTTTGGCATC GTCGGCCTCAACATGAATGGCTACTTTCACGAGGCCTACTTCAAGAAGCACAAGTTCAACACG CACAGGCTGCTCAGTGAGGCTGAGGTTCTGGACCACAGCAAGAACCCTTGTGAAGACTCTTTC CTGCCAGACACAGAGGGCCACACCTACGTGGCCTTTATTCGAATGGAGAAAGATGATGACTTC ACCACCTGGACCCAGCTTGCCAAGTGCCTCCATATCTGGGACCTGGATGTGCGTGGCAACCAT CGGGGCCTGTGGAGATTGTTTCGGAAGAAGAACCACTTCCTGGTGGTGGGGGTCCCGGCTTCC CCCTACTCAGTGAAGAAGCCACCCTCAGTCACCCCAATTTTCCTGGĀGCCACCCCCAAAGGAG GAGGGAGCCCCAGAGCCCCAGAACAGACATGAGACCTCCTCCAGGACCCTGCGGGGCTGGGT ACTGTGTACCCCCAGGCTGGCTAGCCCTTCCCTCCATCCTGTAGGATTTTGTAGATGCTGGTA GGGGCTGGGGCTACCTTGTTTTTAACATGAGACTTAATTACTAACTCCAAGGGGAGGGTTCCC AGGAGAGTACCTGGGAATCATTACGATCCCTAGCAGCTCATCCTGCCCTTTGAATACCCTCAC TTTCCAGGCCTGGCTCAGAATCTAACCTATTTATTGACTGTCCTGAGGGCCTTGAAAACAGGC TTACTCAGGAAACTGCTGTGCCCAACCCATGGACAGGCCCAGCTGGGGCCCACATGCTGACAC AGACTCACTCAGAGACCCTTAGACACTGGACCAGGCCTCCTCTCAGCCTTCTCTTTGTCCAGA AAAAAAAAAAAA

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FIGURE 480

MDDWKPSPLIKPFGARKKRSWYLTWKYKLTNQRALRRFCQTGAVLFLLVTVIVNIKLILDTRR
AISEANEDPEPEQDYDEALGRLEPPRRRGSGPRRVLDVEVYSSRSKVYVAVDGTTVLEDEARE
QGRGIHVIVLNQATGHVMAKRVFDTYSPHEDEAMVLFLNMVAPGRVLICTVKDEGSFHLKDTA
KALLRSLGSQAGPALGWRDTWAFVGRKGGPVFGEKHSKSPALSSWGDPVLLKTDVPLSSAEEA
ECHWADTELNRRRRRFCSKVEGYGSVCSCKDPTPIEFSPDPLPDNKVLNVPVAVIAGNRPNYL
YRMLRSLLSAQGVSPQMITVFIDGYYEEPMDVVALFGLRGIQHTPISIKNARVSQHYKASLTA
TFNLFPEAKFAVVLEEDLDIAVDFFSFLSQSIHLLEEDDSLYCISAWNDQGYEHTAEDPALLY
RVETMPGLGWVLRRSLYKEELEPKWPTPEKLWDWDMWMRMPEQRRGRECIIPDVSRSYHFGIV
GLNMNGYFHEAYFKKHKFNTVPGVQLRNVDSLKKEAYEVEVHRLLSEAEVLDHSKNPCEDSFL
PDTEGHTYVAFIRMEKDDDFTTWTQLAKCLHIWDLDVRGNHRGLWRLFRKKNHFLVVGVPASP
YSVKKPPSVTPIFLEPPPKEEGAPGAPEQT

Important features:

Transmembrane domain:

amino acids 38-55

Homologous region to Mouse GNT1

amino acids 229-660

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FIGURE 481

GAAAGA**ATG**TTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACCA GGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCATAT GCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAAGTT CCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGTATCA TTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACCCCTTCCTGCTGTTGAGGTGCAATCA TTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTGGATTATT ATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTATCAGGGATC TGGCAACGTAGAAGAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGATAAGTGTGAA AACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGGGGGGCATATTA ATGATGCCTTCATGACAGAGGATGAGAGGCTCACCCCTCTCTGAAGGGCTGTTGTTCTGCTTC CTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATACCAAGAGCAGAT CATATATTTTGTTTCACCATTCTTCTTTTGTAATAATTTTGAATGTGCTTGAAAGTGAAAAG CAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGACTCAAAATATTCTAA **AATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTGTAGTTATTGATTTAA** GCATTTTTAGAAATAAGATCAGGCATATGTATATATTTTCACACTTCAAAGACCTAAGGAAAA ATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCATTGAAAATGGATCCTTTT TGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAGTGAGAAGTAATTATTGTA AATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATTTTATCCTGTTATCACACCA ACAGTTGATTATATTTTCTGAATATCAGCCCCTAATAGGACAATTCTATTTGTTGACCATT TCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAGTAATAATCATCTCTTTTTAAA ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

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FIGURE 482

MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVPN REATEISHVLLCNVTQRVSFWFVVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLEFL KIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKCENM ITIENGIPSDPLDMKGGILMMPS

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FIGURE 483

CGTCTCTGCGTTCGCCATGCGTCCCGGGGCGCCAGGGCCACTCTGGCCTCTGCCCTGGGGGGGC CCTGGCTTGGGCCGTGGGCTTCGTGAGCTCCATGGGCTCGGGGAACCCCGCGCCCGGTGGTGT TTGCTGGCTCCAGCAGGGCCAGGAGGCCACCTGCAGCCTGGTGCTCCAGACTGATGTCACCCG CAAGATCAACCTCCTCGGCTTCTTGGGCCTTGTCCACTGCCTTCCCTGCAAAGATTCGTGCGA CGCGCCCGACTGCTCGGGGGCTCCCGGCGGCTGCAGGTCTGCGGCTCAGACGGCGCCACCTA CCGCGACGAGTGCGAGCTGCGCGCGCGCGCGCCGCCCCGGACCTGAGCGTCATGTA CCGGGGCCGCTGCCGCAAGTCCTGTGAGCACGTGGTGTGCCCGCGGCCACAGTCGTGCGTCGT GGACCAGACGGGCAGCGCCCACTGCGTGGTGTGTCGAGCGGCGCCCTGCCCTGTGCCCTCCAG CCCCGGCCAGGAGCTTTGCGGCAACAACAACGTCACCTACATCTCCTCGTGCCACATGCGCCA GGCCACCTGCTTCCTGGGCCGCTCCATCGGCGTGCGCCACGCGGGCAGCTGCGCAGGCACCCC TGAGGAGCCGCCAGGTGGTGAGTCTGCAGAAGAGGAAGAGAACTTCGTG**TGA**GCCTGCAGGAC TAATTTATATGCCACGGACACTCCTTAGAGCCCGGATTCGGACCACTTGGGGATCCCAGAACC AGACCTGCGTTCCGGACACTGAGCGCCTGATTTAGGGCCCCTTCTCTAGGATGCCCCAGCCCCT ACCCTAAGACCTATTGCCGGGGAGGATTCCACACTTCCGCTCCTTTGGGGATAAACCTATTAA TTATTGCTACTATCAAGAGGGCTGGGCATTCTCTGCTGGTAATTCCTGAAGAGGCATGACTGC TTTTCTCAGCCCCAAGCCTCTAGTCTGGGTGTGTACGGAGGGTCTAGCCTGGGTGTGTACGGA GGGTCTAGCCTGGGTGAGTACGGAGGGTCTAGCCTGGGTGAGTACGGAGGGTCTAGCCTGGGT GAGTACGGAGGGTCTAGCCTGGGTGTGTATGGAGGATCTAGCCTGGGTGAGTATGGAGGGTCT AGCCTGGGTGAGTATGGAGGGTCTAGCCTGGGTGTGTATGGAGGGTCTAGCCTGGGTGAGTAT GGAGGGTCTAGCCTGGGTGTGTATGGAGGGTCTAGCCTGGGTGAGTATGGAGGGTCTAGCCTG GGTGTGTACGGAGGGTCTAGTCTGAGTGCGTGTGGGGACCTCAGAACACTGTGACCTTAGCCC AGCAAGCCAGGCCCTTCATGAAGGCCAAGAAGGCTGCCACCATTCCCTGCCAGCCCAAGAACT CCAGCTTCCCCACTGCCTCTGTGTGCCCCTTTGCGTCCTGTGAAGGCCATTGAGAAATGCCCA GTGTGCCCCTGGGAAAGGGCACGGCCTGTGCTCCTGACACGGGCTGTGCTTGGCCACAGAAC CACCCAGCGTCTCCCCTGCTGCTGTCCACGTCAGTTCATGAGGCAACGTCGCGTGGTCTCAGA CGTGGAGCAGCCAGCGCAGCTCAGAGCAGGGCACTGTGTCCGGCGGAGCCAAGTCCACTCTG GGGGAGCTCTGGCGGGGACCACGGGCCACTGCTCACCCACTGGCCCCGAGGGGGGTGTAGACG CCAAGACTCACGCATGTGTGACATCCGGAGTCCTGGAGCCGGGTGTCCCAGTGGCACCACTAG GTGCCTGCTCCCACAGTGGGGTTCACACCCAGGGCTCCTTGGTCCCCCACAACCTGCCCC CTGCGTTGATGCTCAGAATCGCCTACCTGTGCCTGCGTGTAAACCACAGCCTCAGACCAGCTA TGGGGAGAGACACACGGAGGATATCCAGCTTCCCCGGTCTGGGGTGAGGAATGTGGGGAGC TTGGGCATCCTCCAGCCTCCTCCAGCCCCCAGGCAGTGCCTTACCTGTGGTGCCCAGAAA AGTGCCCCTAGGTTGGTGGGTCTACAGGAGCCTCAGCCAGGCAGCCCACCCTGGGGCC CTGCCTCACCAAGGAAATAAAGACTCAAGCCATAAAAAAA

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FIGURE 484

MRPGAPGPLWPLPWGALAWAVGFVSSMGSGNPAPGGVCWLQQGQEATCSLVLQTDVTRAECCA SGNIDTAWSNLTHPGNKINLLGFLGLVHCLPCKDSCDGVECGPGKACRMLGGRPRCECAPDCS GLPARLQVCGSDGATYRDECELRAARCRGHPDLSVMYRGRCRKSCEHVVCPRPQSCVVDQTGS AHCVVCRAAPCPVPSSPGQELCGNNNVTYISSCHMRQATCFLGRSIGVRHAGSCAGTPEEPPG GESAEEEENFV

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation sites.

amino acids 73-77, 215-219

Osteonectin domain proteins.

amino acids 97-130, 169-202

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FIGURE 485

GCTCGAGGCCGGCGGCGGGGAGAGCGACCCGGGCGCCTCGTAGCGGGGCCCCGGATCCCC GAGTGGCGGCCGGAGCCTCGAAAAGAGATTCTCAGCGCTGATTTTGAGATGATGGGCTTGGGA AACGGGCGTCGCAGCATGAAGTCGCCGCCCCTCGTGCTGGCCGCCCTGGTGGCCTGCATCATC GTCTTGGGCTTCAACTACTGGATTGCGAGCTCCCGGAGCGTGGACCTCCAGACACGGATCATG GAGCTGGAAGGCAGGGTCCGCAGGGCGCTGCAGAGAGAGGCGCCGTGGAGCTGAAGAAGAAC GAGTTCCAGGGAGAGCTGGAGAAGCAGCGGGAGCAGCTTGACAAAATCCAGTCCAGCCACAAC TTCCAGCTGGAGAGCGTCAACAAGCTGTACCAGGACGAAAAGGCGGTTTTGGTGAATAACATC ACCACAGGTGAGAGGCTCATCCGAGTGCTGCAAGACCAGTTAAAGACCCTGCAGAGGAATTAC GGCAGGCTGCAGCAGGTGTCCTCCAGTTTCAGAAGAACCAGACCAACCTGGAGAGGAAGTTC TCCTACGACCTGAGCCAGTGCATCAATCAGATGAAGGAGGTGAAGGAACAGTGTGAGGAGCGA ATAGAAGAGGTCACCAAAAAGGGGAATGAAGCTGTAGCTTCCAGAGACCTGAGTGAAAACAAC CCACACACAGAGGTGCCACAAGGGAAGGGAAACGTGCTTGGTAACAGCAAGTCCCAGACACCA GCCCCCAGTTCCGAAGTGGTTTTGGATTCAAAGAGACAAGTTGAGAAAGAGGAAACCAATGAG ATCCAGGTGGTGAATGAGGAGCCTCAGAGGGACAGGCTGCCGCAGGAGCCAGGCCGGGAGCAG GTGGTGGAAGACCTGTAGGTGGAAGAGGCTTCGGGGGAGCCGGAGAACTGGGCCAGACC CCACAGGTGCAGGCTGCCCTGTCAGTGAGCCAGGAAAATCCAGAGATGGAGGGCCCTGAGCGA GACCAGCTTGTCATCCCCGACGGACAGGAGGAGGAGGAGCAGGAAGCTGCCGGGGAAGGGAGAAAC CAGCAGAAACTGAGAGGAGAAGATGACTACAACATGGATGAAAATGAAGCAGAATCTGAGACA GACAAGCAAGCCCTGGCAGGGAATGACAGAAACATAGATGTTTTTAATGTTGAAGATCAG AAAAGAGACACCATAAATTTACTTGATCAGCGTGAAAAGCGGAATCATACACTC**TGA**ATTGAA CTGGAATCACATATTTCACAACAGGGCCGAAGAGATGACTATAAAATGTTCATGAGGGACTGA ATACTGAAAACTGTGAAATGTACTAAATAAAATGTACATCTGA

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FIGURE 486

MMGLGNGRRSMKSPPLVLAALVACIIVLGFNYWIASSRSVDLQTRIMELEGRVRRAAAERGAV ELKKNEFQGELEKQREQLDKIQSSHNFQLESVNKLYQDEKAVLVNNITTGERLIRVLQDQLKT LQRNYGRLQQDVLQFQKNQTNLERKFSYDLSQCINQMKEVKEQCEERIEEVTKKGNEAVASRD LSENNDQRQQLQALSEPQPRLQAAGLPHTEVPQGKGNVLGNSKSQTPAPSSEVVLDSKRQVEK EETNEIQVVNEEPQRDRLPQEPGREQVVEDRPVGGRGFGGAGELGQTPQVQAALSVSQENPEM EGPERDQLVIPDGQEEEQEAAGEGRNQQKLRGEDDYNMDENEAESETDKQAALAGNDRNIDVF NVEDQKRDTINLLDQREKRNHTL

Important features:

Signal peptide:

amino acids 1-29

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FIGURE 487

AACTCAAACTCCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGGG ${\tt TGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTC} {\tt ATG} {\tt TAT}$ GGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATACAGCTCACAGCTCTTTGGCCT ATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGCTCGG TTAAAATGCACTTTCTCCAGCTTTGCCCCTGTGGGTGATGCTCTAACAGTGACCTGGAATTTT CGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTCCAACCC ATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGATGCCTCC ATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGAAGAACCCA CCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTACGCTTCTCT GAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCATAATAGTAATT GTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTCATAAAGTGGTG GACACAGAC<u>TAA</u>CAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAAGAACCCTAGTATT TCTTGAAGTTAATGGAAACTTTTCTTTGGCTTTTTCCAGTTGTGACCCGTTTTCCAACCAGTTC TGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCACAGTGCTCCTCCATAT CACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGAGTGTAAATTTTTTCAA GTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAAGACACTACTTACAGTGT TATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCCAATTTGTCTGTTACATTT CCTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTAATGTGTTTACTCTCTTTCC TTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTGTTTCTGATTAACAGTAAATC CTAAATTCAAACTGTTAAATGACATTTTTATTTTTTATGTCTCTCTTAACTATGAGACACATC TTGTTTTACTGAATTTCTTTCAATATTCCAGGTGATAGATTTTTGTCG

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FIGURE 488

MYGKSSTRAVLLLLGIQLTALWPIAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVTW
NFRPLDGGPEQFVFYYHIDPFQPMSGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQVK
NPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVLFQHYRKKRWAERAHK
VVEIKSKEEERLNQEKKVSVYLEDTD

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FIGURE 489

AAGCAACCAAACTGCAAGCTTTGGGAGTTGTTCGCTGTCCCTGCCCTGCTCTGCTAGGGAGAG AACGCCAGAGGGAGGCGGCTGGCCCGGCGGCAGGCTCTCAGAACCGCTACCGGCGATGCTACT GCTGTGGGTGTCGCTGGCCAGCCTTGGCGCTGGCGGTACTGGCCCCCGGAGCAGGGGAGCA GAGGCGGAGAGCAGCCAAAGCGCCCAATGTGGTGCTGGTCGTGAGCGACTCCTTCGATGGAAG GTTAACATTTCATCCAGGAAGTCAGGTAGTGAAACTTCCTTTTATCAACTTTATGAAGACACG TGGGACTTCCTTTCTGAATGCCTACACAAACTCTCCAATTTGTTGCCCATCACGCGCAGCAAT GTGGAGTGGCCTCTTCACTCACTTAACAGAATCTTGGAATAATTTTAAGGGTCTAGATCCAAA TTATACAACATGGATGGATGTCATGGAGAGGCATGGCTACCGAACACAGAAATTTGGGAAACT GGACTATACTTCAGGACATCACTCCATTAGTAATCGTGTGGAAGCGTGGACAAGAGATGTTGC TTTCTTACTCAGACAAGAAGGCAGGCCCATGGTTAATCTTATCCGTAACAGGACTAAAGTCAG AGTGATGGAAAGGGATTGGCAGAATACAGACAAAGCAGTAAACTGGTTAAGAAAGGAAGCAAT TAATTACACTGAACCATTTGTTATTTACTTGGGATTAAATTTACCACACCCTTACCCTTCACC ATCTTCTGGAGAAAATTTTGGATCTTCAACATTTCACACATCTCTTTATTGGCTTGAAAAAGT GTCTCATGATGCCATCAAAATCCCAAAGTGGTCACCTTTGTCAGAAATGCACCCTGTAGATTA AGCATTTTATTATGCTATGTGTGCTGAGACAGATGCCATGCTTGGTGAAATTATTTTGGCCCT TCATCAATTAGATCTTCTTCAGAAAACTATTGTCATATACTCCTCAGACCATGGAGAGCTGGC CATGGAACATCGACAGTTTTATAAAATGAGCATGTACGAGGCTAGTGCACATGTTCCGCTTTT GATGATGGGACCAGGAATTAAAGCCGGCCTACAAGTATCAAATGTGGTTTCTCTTGTGGATAT TTACCCTACCATGCTTGATATTGCTGGAATTCCTCTGCCTCAGAACCTGAGTGGATACTCTTT GTTGCCGTTATCATCAGAAACATTTAAGAATGAACATAAAGTCAAAAACCTGCATCCACCCTG GATTCTGAGTGAATTCCATGGATGTAATGTGAATGCCTCCACCTACATGCTTCGAACTAACCA CTGGAAATATATAGCCTATTCGGATGGTGCATCAATATTGCCTCAACTCTTTGATCTTTCCTC GGATCCAGATGAATTAACAAATGTTGCTGTAAAATTTCCAGAAATTACTTATTCTTTGGATCA GAAGCTTCATTCCATTATAAACTACCCTAAAGTTTCTGCTTCTGTCCACCAGTATAATAAAGA GCAGTTTATCAAGTGGAAACAAAGTATAGGACAGAATTATTCAAACGTTATAGCAAATCTTAG GTGGCACCAAGACTGGCAGAAGGAACCAAGGAAGTATGAAAATGCAATTGATCAGTGGCTTAA AACCCATATGAATCCAAGAGCAGTT<u>TGA</u>ACAAAAAGTTTAAAAATAGTGTTCTAGAGATACAT ATAAATATATTACAAGATCATAATTATGTATTTTAAATGAAACAGTTTTAATAATTACCAAGT TTTGGCCGGGCACAGTGGCTCACACCTGTAATCCCAGGACTTTGGGAGGCTGAGGAAAGCAGA TCACAAGGTCAAGAGATTGAGACCATCCTGGCCAACATGGTGAAACCCTGTCTCTACTAAAAA TACAAAAATTAGCTGGGCGCGGTGGTGCACACCTATAGTCTCAGCTACTCAGAGGCTGAGGCA GGAGGATCGCTTGAACCCGGGAGGCAGCAGTTGCAGTGAGCTGAGATTGCGCCACTGTACTCC AGCCTGGCAACAGAGTGAGACTGTGTCGCAAAAAAATAAAAATAAAATAATAATAATTACCAA TTTTTCATTATTTTGTAAGAATGTAGTGTATTTTAAGATAAAATGCCAATGATTATAAAATCA CATATTTTCAAAAATGGTTATTATTTAGGCCTTTGTACAATTTCTAACAATTTAGTGGAAGTA TCAAAAGGATTGAAGCAAATACTGTAACAGTTATGTTCCTTTAAATAATAGAGAATATAAAAAT AAAAAAAAAAAAAAA

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FIGURE 490

MLLLWVSVVAALALAVLAPGAGEQRRRAAKAPNVVLVVSDSFDGRLTFHPGSQVVKLPFINFM
KTRGTSFLNAYTNSPICCPSRAAMWSGLFTHLTESWNNFKGLDPNYTTWMDVMERHGYRTQKF
GKLDYTSGHHSISNRVEAWTRDVAFLLRQEGRPMVNLIRNRTKVRVMERDWQNTDKAVNWLRK
EAINYTEPFVIYLGLNLPHPYPSPSSGENFGSSTFHTSLYWLEKVSHDAIKIPKWSPLSEMHP
VDYYSSYTKNCTGRFTKKEIKNIRAFYYAMCAETDAMLGEIILALHQLDLLQKTIVIYSSDHG
ELAMEHRQFYKMSMYEASAHVPLLMMGPGIKAGLQVSNVVSLVDIYPTMLDIAGIPLPQNLSG
YSLLPLSSETFKNEHKVKNLHPPWILSEFHGCNVNASTYMLRTNHWKYIAYSDGASILPQLFD
LSSDPDELTNVAVKFPEITYSLDQKLHSIINYPKVSASVHQYNKEQFIKWKQSIGQNYSNVIA
NLRWHQDWQKEPRKYENAIDQWLKTHMNPRAV

Important features:

Signal peptide:

amino acids 1-15

N-glycosylation sites.

amino acids 108-111, 166-169, 193-196, 262-265, 375-378, 413-416, 498-501

Sulfatases proteins:

amino acids 286-315, 359-369, 78-97

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FIGURE 491

GAGAGAGTCAGCCTGGCAGAGAGACTCTGAAATGAGGGATTAGAGGTGTTCAAGGAGCAAGA GCTTCAGCCTGAAGACAAGGGAGCAGTCCCTGAAGACGCTTCTACTGAGAGGTCTGCC**AT**GGC CTCTCTTGGCCTCCAACTTGTGGGCTACATCCTAGGCCTTCTGGGGCTTTTTGGGCACACTGGT TGCCATGCTGCTCCCCAGCTGGAAAACAAGTTCTTATGTCGGTGCCAGCATTGTGACAGCAGT CATCTATAGCACCCTTCTGGGCCTGCCCGCTGACATCCAGGCTGCCCAGGCCATGATGGTGAC ATCCAGTGCAATCTCCTCCCTGGCCTGCATTATCTCTGTGGTGGGCATGAGATGCACAGTCTT CTGCCAGGAATCCCGAGCCAAAGACAGAGTGGCGGTAGCAGGTGGAGTCTTTTTCATCCTTGG AGGCCTCCTGGGATTCATTCCTGTTGCCTGGAATCTTCATGGGATCCTACGGGACTTCTACTC ACCACTGGTGCCTGACAGCATGAAATTTGAGATTGGAGAGGCTCTTTACTTGGGCATTATTTC TTCCCTGTTCTCCCTGATAGCTGGAATCATCCTCTGCTTTTCCTGCTCATCCCAGAGAAATCG CTCCAACTACTACGATGCCTACCAAGCCCAACCTCTTGCCACAAGGAGCTCTCCAAGGCCTGG TCAACCTCCCAAAGTCAAGAGTGAGTTCAATTCCTACAGCCTGACAGGGTATGTG**TGA**AGAAC CAGGGGCCAGAGCTGGGGGGGGGGCTGGGTCTGTGAAAAACAGTGGACAGCACCCCGAGGGCCA CCATTGGATTGAGCAAAGGCAGAAATGGGGGCTAGTGTAACAGCATGCAGGTTGAATTGCCAA GGATGCTCGCCATGCCAGCCTTTCTGTTTTCCTCACCTTGCTGCTCCCCTGCCCTAAGTCCCC AACCCTCAACTTGAAACCCCATTCCCTTAAGCCAGGACTCAGAGGATCCCTTTGCCCTCTGGT AGACCCTCTCTCTGGCTGAGGTTGGCTCTTAGCTCATTGCTGGGGATGGGAAGGAGAAGCAGT GGCTTTTGTGGGCATTGCTCTAACCTACTTCTCAAGCTTCCCTCCAAAGAAACTGATTGGCCC TGGAACCTCCATCCCACTCTTGTTATGACTCCACAGTGTCCAGACTAATTTGTGCATGAACTG AAATAAAACCATCCTACGGTATCCAGGGAACAGAAAGCAGGATGCAGGATGGGAGGACAGGAA GGCAGCCTGGGACATTTAAAAAAATA

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FIGURE 492

MASLGLQLVGYILGLLGLLGTLVAMLLPSWKTSSYVGASIVTAVGFSKGLWMECATHSTGITQ CDIYSTLLGLPADIQAAQAMMVTSSAISSLACIISVVGMRCTVFCQESRAKDRVAVAGGVFFI LGGLLGFIPVAWNLHGILRDFYSPLVPDSMKFEIGEALYLGIISSLFSLIAGIILCFSCSSQR NRSNYYDAYQAQPLATRSSPRPGQPPKVKSEFNSYSLTGYV

Important features:

Signal peptide:

amino acids 1-24

Transmembrane domains:

amino acids 82-102, 117-140, 163-182

N-glycosylation site.

amino acids 190-193

PMP-22 / EMP / MP20 family proteins.

amino acids 46-59

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FIGURE 493

GCACTGCTGCTCCCATCAGCTGCTCTGAAGCTCCATGGTGCCCAGAATCTTCGCTCCTGCT
TATGTGTCAGTCTGTCTCCTCCTCTTGTGTCCAAGGGAAGTCATCGCTCCCGCTGGCTCAGAA
CCATGGCTGTGCCAGCCGGCACCCAGGTGTGGAGACAAGATCTACAACCCCTTGGAGCAGTGC
TGTTACAATGACGCCATCGTGTCCCTGAGCGAGACCCGCCAATGTGGTCCCCCCTGCACCTTC
TGGCCCTGCTTTGAGCTCTGTCTTGATTCCTTTGGCCTCACAAACGATTTTGTTGTGAAG
CTGAAGGTTCAGGGTGTGAATTCCCAGTGCCACTCATCTCCCATCTCCAGTAAATGTGAAAGC
AGAAGACGTTTTCCCTGAGAAAGAAAAATCAACTTTCACTAAGGCATCTCAGAAA
CATAGGCTAAGGTAATATGTGTACCAGTAGAGAAGCCTGAGGAATTTACAAAATGATGCAGCT
CCAAGCCATTGTATGGCCCATGTGGGAGACTGATGGAGAATGACAGTAGATTATCA
GGAAATAAATAAAGTGGTTTTTCCAATGTACACACCTGTAAAA

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FIGURE 494

 ${\tt MVPRIFAPAYVSVCLLLLCPREVIAPAGSEPWLCQPAPRCGDKIYNPLEQCCYNDAIVSLSET} \\ {\tt RQCGPPCTFWPCFELCCLDSFGLTNDFVVKLKVQGVNSQCHSSPISSKCESRRRFP}$

Important features:

Signal peptide:

amino acids 1-25

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FIGURE 495

CTCCACTGCAACCACCCAGAGCCATGGCTCCCCGAGGCTGCATCGTAGCTGTCTTTGCCATTT
TCTGCATCTCCAGGCTCCTCTGCTCACACGGAGCCCCAGTGGCCCCCATGACTCCTTACCTGA
TGCTGTGCCAGCCACACAAGAGATGTGGGGACCAAGTTCTACGACCCCCTGCAGCACTGTTGCT
ATGATGATGCCGTCGTGCCCTTGGCCAGGACCCAGACGTGTGGAAACTGCACCTTCAGAGTCT
GCTTTGAGCAGTGCTGCCCCTGGACCTTCATGGTGAAGCTGATAAACCAGAACTGCGACTCAG
CCCGGACCTCGGATGACAGGCTTTGTCGCAGTGTCAGCTAATGGAACATCAGGGGAACGATGA
CTCCTGGATTCTCCTTCCTGGGTGGGCCTGGAGAAAGAGGCTGGTGTTACCTGAGATCTGGGA
TGCTGAGTGGCTGTTTGGGGGCCCAGAGAAACACACCTCAACTGCCCACTTCATTCTGTGACC
TGTCTGAGGCCCACCCTGCAGCTGCCCTGAGGAGCCCACAGGTCCCCTTCTAGAATTCTGGA
CAGCATGAGATGCGTGTGCTGATGGGGGCCCAGGGACCTCCACCCTTCATGACCCCCTATG
GCCAACATCAACCCGGCACCACCCCAAGGCTGGCTGGGGAACCCTTCACCCTTCTGTGAGATT
TTCCATCATCTCAAGTTCTCTTCTATCCAGGAGCAAAGCACAGGATCATAATAAATTTATGTA
CTTTATAAATGAAAA

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FIGURE 496

MAPRGCIVAVFAIFCISRLLCSHGAPVAPMTPYLMLCQPHKRCGDKFYDPLQHCCYDDAVVPL ARTQTCGNCTFRVCFEQCCPWTFMVKLINQNCDSARTSDDRLCRSVS

Important features:

Signal peptide:

amino acids 1-24

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FIGURE 497

TGAAGGACTTTTCCAGGACCCAAGGCCACACTGGAAGTCTTGCAGCTGAAGGGAGGCACTC CTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGTCCTCCTGGC ACAGGTGTGGCTGGTACCCGGCTTGGCCCCCAGTCCTCAGTCGCCAGAGACCCCAGCCCCTCA GAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGGCCAG GGAGACTTCAAACTTCGGATTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGGCAACAT GGTCTTCTCTCCATTTGGCATGTCCTTGGCCATGACAGGCTTGATGCTGGGGGCCACAGGGCC GACTGAAACCCAGATCAAGAGAGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAGCCCGGGCT CCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAACTGGGCCTCTC ACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCTTCAATTTATC CAAGAGGTATTTTGATACAGAGTGCGTGCCTATGAATTTTCGCAATGCCTCACAGGCCAAAAG GCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTCCCAAACTGTTTGATGAGAT TAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGAAATGGTTGACCCC ATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTACAAGACCATTAAGGT GCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAATTTTCGTTGTCATGT CCTCAAACTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCCTCATGGAGAAAATGGGTGA CCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACATGGCTCAGAAACATGAA AACCAGAAACATGGAAGTTTTCTTTCCGAAGTTCAAGCTAGATCAGAAGTATGAGATGCATGA GCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCTTTGCTGACCTTAGTGAACTCTC AGCTACTGGAAGAATCTCCAAGTATCCAGGGTTTTACGAAGAACAGTGATTGAAGTTGATGA AAGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTACTGCTTATTCCATGCCTCCTGT CATCAAAGTGGACCGGCCATTTCATTTCATGATCTATGAAGAAACCTCTGGAATGCTTCTGTT TCTGGGCAGGGTGGTGAATCCGACTCTCCTA**TAA**TTCAGGACATGCATAAGCACTTCGTGCTG TCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGCCTGAAACGGTGGACAGTGCTGAACCT TATATATATTTTTCCTACACATACATACCTATGATAAAGTTTAATTTATAAATTAGGCACAG TAAGAGATTAACAATAATAACAACATTAAGTAAAATGAGTTACTTGAACGCAAGCACTGCAAT ACCATAACAGTCAAACTGATTATAGAGAAGGCTACTAAGTGACTCATGGGCGAGGAGCATAGA AAGATTCCATCCCACTACTCAGAATGGCATGCTGCTTAAGACTTTTAGATTGTTTATTTCTGG AATTTTTCATTTAATGTTTTTGGACCATGGTTGACCATGGTTAACTGAGACTGCAGAAAGCAA AACCATGGATAAGGGAGGACTACTACAAAAGCATTAAATTGATACATATTTTTTAAAAAÁAAA AAAAAAAAA

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FIGURE 498

MKVVPSLLLSVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEEDEQEASEEKAGEE
EKAWLMASRQQLAKETSNFGFSLLRKISMRHDGNMVFSPFGMSLAMTGLMLGATGPTETQIKR
GLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYFDTE
CVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTPFDPVFTE
VDTFHLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHLALEDY
LTTDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRIFSPFADLSELSATGRNLQ
VSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLFLGRVVNP
TLL

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FIGURE 499

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FIGURE 500

 ${\tt MDSLRKMLISVAMLGAGAGVGYALLVIVTPGERRKQEMLKEMPLQDPRSREEAARTQQLLLAT} \\ {\tt LQEAATTQENVAWRKNWMVGGEGGASGRSP}$

Important features:

Signal peptide:

amino acids 1-18

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FIGURE 501

CAGGAGAGAGGCACCGCCCCACCCGCCTCCAAAGCTAACCCTCGGGCTTGAGGGGAAGAG GCTGACTGTACGTTCCTTCTACTCTGGCACCACTCTCCAGGCTGCCATGGGGCCCAGCACCCC TCTCCTCATCTTGTTCCTTTTGTCATGGTCGGGACCCCTCCAAGGACAGCAGCACCCTTGT GGAGTACATGGAACGCCGACTAGCTGCTTTAGAGGAACGGCTGGCCCAGTGCCAGGACCAGAG TAGTCGGCATGCTGAGCTGCGGGACTTCAAGAACAAGATGCTGCCACTGCTGGAGGTGGC AGAGAAGGAGCGGGAGGCACTCAGAACTGAGGCCGACACCATCTCCGGGAGAGTGGATCGTCT GGAGCGGGAGGTAGACTATCTGGAGACCCAGAACCCAGCTCTGCCCTGTGTAGAGTTTGATGA GAAGGTGACTGGAGGCCCTGGGACCAAAGGCAAGGGAAGAAGGAATGAGAAGTACGATATGGT GACAGACTGTGGCTACACAATCTCTCAAGTGAGATCAATGAAGATTCTGAAGCGATTTGGTGG CCCAGCTGGTCTATGGACCAAGGATCCACTGGGGCAAACAGAGAAGATCTACGTGTTAGATGG GACACAGAATGACACAGCCTTTGTCTTCCCAAGGCTGCGTGACTTCACCCTTGCCATGGCTGC CCGGAAAGCTTCCCGAGTCCGGGTGCCCTTCCCCTGGGTAGGCACAGGGCAGCTGGTATATGG TGGCTTTCTTTATTTTGCTCGGAGGCCTCCTGGAAGACCTGGTGGAGGTGGTGAGATGGAGAA CACTTTGCAGCTAATCAAATTCCACCTGGCAAACCGAACAGTGGTGGACAGCTCAGTATTCCC AGCAGAGGGGCTGATCCCCCCCTACGGCTTGACAGCAGACACCTACATCGACCTGGTAGCTGA TGAGGAAGGTCTTTGGGCTGTCTATGCCACCCGGGAGGATGACAGGCACTTGTGTCTGGCCAA GTTAGATCCACAGACACTGGACACAGAGCAGCAGTGGGACACCATGTCCCAGAGAGAATGC TGAGGCTGCCTTTGTCATCTGTGGGACCCTCTATGTCGTCTATAACACCCGTCCTGCCAGTCG GGCCCGCATCCAGTGCTCCTTTGATGCCAGCGGCACCCTGACCCCTGAACGGGCAGCACTCCC TTATTTCCCCGCAGATATGGTGCCCATGCCAGCCTCCGCTATAACCCCCGAGAACGCCAGCT GGTT**TGA**GGAGCTAGCCTTGTTTTTTGCATCTTTCTCACTCCCATACATTTATATTATATCCC CACTAAATTTCTTGTTCCTCATTCTTCAAATGTGGGCCAGTTGTGGCTCAAATCCTCTATATT TTTAGCCAATGGCAATCAAATTCTTTCAGCTCCTTTGTTTCATACGGAACTCCAGATCCTGAG TAATCCTTTTAGAGCCCGAAGAGTCAAAACCCTCAATGTTCCCTCCTGCTCTCCTGCCCCATG TCAACAAATTTCAGGCTAAGGATGCCCCAGACCCAGGGCTCTAACCTTGTATGCGGGCAGGCC CAGGGAGCAGCAGTGTTCTTCCCCTCAGAGTGACTTGGGGAGGAGAAATAGGAGGAGA CGTCCAGCTCTGTCCTCTCTCCTCACTCCTTCAGTGTCCTGAGGAACAGGACTTTCTC

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FIGURE 502

MGPSTPLLILFLLSWSGPLQGQQHHLVEYMERRLAALEERLAQCQDQSSRHAAELRDFKNKML
PLLEVAEKEREALRTEADTISGRVDRLEREVDYLETQNPALPCVEFDEKVTGGPGTKGKGRRN
EKYDMVTDCGYTISQVRSMKILKRFGGPAGLWTKDPLGQTEKIYVLDGTQNDTAFVFPRLRDF
TLAMAARKASRVRVPFPWVGTGQLVYGGFLYFARRPPGRPGGGGEMENTLQLIKFHLANRTVV
DSSVFPAEGLIPPYGLTADTYIDLVADEEGLWAVYATREDDRHLCLAKLDPQTLDTEQQWDTP
CPRENAEAAFVICGTLYVVYNTRPASRARIQCSFDASGTLTPERAALPYFPRRYGAHASLRYN
PRERQLYAWDDGYQIVYKLEMRKKEEEV

Important features:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 177-180, 248-251

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FIGURE 503

TGCGGCGCAGTGTAGACCTGGGAGGATGGGCCGCCTGCTGCTGCTGCTTTTCTGGCTTTGGT
CTCGGTGCCCAGGGCCCAGGCCGTGTGGTTGGGAAGACTGGACCCTGAGCAGCTTCTTGGGCC
CTGGTACGTGCTTGCGGTGGCCTCCCGGGAAAAGGGCTTTTGCCATGGAGAAGGACATGAAGAA
CGTCGTGGGGGTGGTGACCCTCACTCCAGAAAACAACCTGCGGACGCTGTCCTCTCAGCA
CGGGCTGGGAGGGTGTGACCAGAGTGTCATGGACCTGATAAAGCGAAACTCCGGATGGGTGTT
TGAGAATCCCTCAATAGGCGTGCTGGAGCTCTGGGTGCTGCCACCAACTTCAGAGACTATGC
CATCATCTTCACTCAGCTGGAGTTCGGGGACGCCCTTCAACACCGTGGAGCTGTACAGTCT
GACGGAGACAGCCAGCCAGGAGGCCCATGGGGCTCTTCACCAAGTGGAGCCTGGGCTT
CCTGTCACAGTAGCAGCCAGCAGCAGAAGGACCTCACCTGTGCTCACAAGATCCTTCTGTG
AGTGCTGCGTCCCCAGTAGGGATGGCGCCCACAGGGTCCTGTGACCTCGGCCAGTGTCCACCC
ACCTCGCTCAGCGGCTCCCGGGGCCCAGCACCAGCTCAGAATAAAGCGATTCCACAGCA

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FIGURE 504

MGGLLLAAFLALVSVPRAQAVWLGRLDPEQLLGPWYVLAVASREKGFAMEKDMKNVVGVVVTL TPENNLRTLSSQHGLGGCDQSVMDLIKKNSGWVFENPSIGVLELWVLATNFRDYAIIFTQLEF GDEPFNTVELYSLTETASQEAMGLFTKWSRSLGFLSQ

Important features:

Signal peptide:

amino acids 1-20

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FIGURE 505

GTTCCGCAGATGCAGAGGTTGAGGTGGCTGCGGGACTGGAAGTCATCGGGCAGAGGTCTCACA GCAGCCAAGGAACCTGGGGCCCGCTCCTCCCCCCTCCAGGCC**ATG**AGGATTCTGCAGTTAATC CTGCTTGCTCTGGCAACAGGGCTTGTAGGGGGAGAGACCAGGATCATCAAGGGGTTCGAGTGC AAGCCTCACTCCCAGCCCTGGCAGGCAGCCCTGTTCGAGAAGACGCGGCTACTCTGTGGGGCG ACGCTCATCGCCCCAGATGGCTCCTGACAGCAGCCCACTGCCTCAAGCCCCGCTACATAGTT CACCTGGGGCAGCACAACCTCCAGAAGGAGGAGGGCTGTGAGCAGACCCGGACAGCCACTGAG TCCTTCCCCCACCCGGCTTCAACAACAGCCTCCCCAACAAGACCACCGCAATGACATCATG CTGGTGAAGATGGCATCGCCAGTCTCCATCACCTGGGCTGTGCGACCCCTCACCCTCTCCTCA CGCTGTGTCACTGCTGGCACCAGCTGCCTCATTTCCGGCTGGGGCAGCACGTCCAGCCCCCAG TTACGCCTGCCTCACACCTTGCGATGCGCCAACATCACCATCATTGAGCACCAGAAGTGTGAG AACGCCTACCCGGCAACATCACAGACACCATGGTGTGTGCCAGCGTGCAGGAAGGGGGCAAG GACTCCTGCCAGGGTGACTCCGGGGGCCCTCTGGTCTGTAACCAGTCTCTTCAAGGCATTATC TCCTGGGGCCAGGATCCGTGTGCGATCACCCGAAAGCCTGGTGTCTACACGAAAGTCTGCAAA TATGTGGACTGGATCCAGGAGACGATGAAGAACAAT<u>TAG</u>ACTGGACCCACCCACCACACACCCA TCACCCTCCATTTCCACTTGGTGTTTGGTTCCTGTTCACTCTGTTAATAAGAAACCCTAAGCC AAGACCCTCTACGAACATTCTTTGGGCCTCCTGGACTACAGGAGATGCTGTCACTTAATAATC AACCTGGGGTTCGAAATCAGTGAGACCTGGATTCAAATTCTGCCTTGAAATATTGTGACTCTG GGAATGACACCCTGGTTTGTTCTCTGTTGTATCCCCAGCCCCAAAGACAGCTCCTGGCCAT AAAAAA

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FIGURE 506

MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTAAHC LKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPVSITWAV RPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPGNITDTMVCA SVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDPCAITRKPGVYTKVCKYVDWIQETMKNN

Important features:

Signal peptide:

amino acids 1-18

Serine proteases, trypsin family, histidine active site. amino acids 58-63

N-glycosylation sites.

amino acids 99-102, 165-168, 181-184, 210-213

Glycosaminoglycan attachment site.

amino acids 145-148

Kringle domain proteins.

amino acids 197-209, 47-64

Serine proteases, trypsin family, histidine protein

amino acids 199-209, 47-63, 220-243

Apple domain proteins

amino acids 222-249, 189-222

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FIGURE 507

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FIGURE 508

MRRLLLVTSLVVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVLF PVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEERP RLWVMPNHQVLLGPEEDQDHIYHPQ

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FIGURE 509

ACGAGGCTGCCGCATCCTGCCCTCGGAACA**ATG**GGACTCGGCGCGAGGTGCTTGGGCCGCG CTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGGCCCCCATGAAAGCGCAGCCATG GCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACTCCAGTGCTAACTCAACAGAG ACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAACCACCA ACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCGGCATCT AATACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTCTACACCC AAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCGTAACCCAC AATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACTATGCATTCTGAAGCA AAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAACGCTGGGAGTT TTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTCGGTATCGAACC ATAGATGAACATGATGCCATCATT**TAA**GGAAATCCATGGACCAAGGATGGAATACAGATTGAT GCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCTCTTTTTGAAAATA GTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTAAAGATTCTTCAAGG TAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGTTCATACAATGGTTTT TCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAATGCCATCTGGGCATACA AATAAGAAGTTTGTCACAGCACTCAGGATTTTGGGTATCTTTTGTAGCTCACATAAAGAACTT CAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACACAGAAATTATACAATCAAA CTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTTGTGCTTTAAACTGTAGTAGTT **GGTCTAGAAACAAAATACTCC**

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FIGURE 510

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPHNSSANSTETLQHVPSDHT
NETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSVSQNTS
QISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSILYIGCKM
YYSRRGIRYRTIDEHDAII

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FIGURE 511

GACTTTGCTTGAATGTTTACATTTTCTGCTCGCTGTCCTACATATCACAATATAGTGTTCACGTTTTGTTAAAAC $\tt TTTGGGGTGTCAGGAGTTGAGCTTGCTCAGCAAGCCAGCATGGCTAGGATGAGCTTTGTTATAGCAGCTTGCCAA \ . \\$ TGTGAAATTCGTCCCTGGTTTACCCCACAGTCAACTTACAGAGAAGCCACCACTGTTGATTGCAATGACCTCCGC TTAACAAGGATTCCCAGTAACCTCTCTAGTGACACACAAGTGCTTCTCTTACAGAGCAATAACATCGCGAAGACT GTGGATGAGCTGCAGCAGCTTTTCAACTTGACTGAACTAGATTTCTCCCCAAAACAACTTTACTAACATTAAGGAG GTCGGGCTGGCAAACCTAACCCAGCTCACAACGCTGCATTTGGAGGAAAATCAGATTACCGAGATGACTGATTAC TGTCTACAAGACCTCAGCAACCTTCAAGAACTCTACATCAACCACAACCAAATTAGCACTATTTCTGCTCATGCT TTTGCAGGCTTAAAAAATCTATTAAGGCTCCACCTGAACTCCAACAAATTGAAAGTTATTGATAGTCGCTGGTTT GATTCTACACCCAACCTGGAAATTCTCATGATCGGAGAAAACCCTGTGATTGGAATTCTGGATATGAACTTCAAA CCCCTCGCAAATTTGAGAAGCTTAGTTTTGGCAGGAATGTATCTCACTGATATTCCTGGAAATGCTTTGGTGGGT CTGGATAGCCTTGAGAGCCTGTCTTTTTATGATAACAAACTGGTTAAAGTCCCTCAACTTGCCCTGCAAAAAGTT CCAAATTTGAAATTCTTAGACCTCAACAAAAACCCCATTCACAAAAATCCAAGAAGGGGACTTCAAAAATATGCTT CGGTTAAAAGAACTGGGAATCAACAATATGGGCGAGCTCGTTTCTGTCGACCGCTATGCCCTGGATAACTTGCCT GAACTCACAAAGCTGGAAGCCACCAATAACCCTAAACTCTCTTACATCCACCGCTTGGCTTTCCGAAGTGTCCCT CTGCGTGAGATCAGTATCCATAGCAATCCCCTCAGGTGTGACTGTGTGATCCACTGGATTAACTCCAACAAAACC AACATCCGCTTCATGGAGCCCCTGTCCATGTTCTGTGCCATGCCGCCCGAATATAAAGGGCACCAGGTGAAGGAA GTTTTAATCCAGGATTCGAGTGAACAGTGCCTCCCAATGATATCTCACGACAGCTTCCCAAATCGTTTAAACGTG GATATCGGCACGACGGTTTTCCTAGACTGTCGAGCCATGGCTGAGCCAGAACCTGAAATTTACTGGGTCACTCCC ATTGGAAATAAGATAACTGTGGAAACCCTTTCAGATAAATACAAGCTAAGTAGCGAAGGTACCTTGGAAATATCT AACATACAAATTGAAGACTCAGGAAGATACACATGTGTTGCCCAGAATGTCCAAGGGGCAGACACTCGGGTGGCA TCCATCTTAGTGTCCTGGAAAGTTAATTCCAATGTCATGACGTCAAACTTAAAATGGTCGTCTGCCACCATGAAG ATTGATAACCCTCACATAACATATACTGCCAGGGTCCCAGTCGATGTCCATGAATACAACCTAACGCATCTGCAG CCTTCCACAGATTATGAAGTGTGTCTCACAGTGTCCAATATTCATCAGCAGACTCAAAAGTCATGCGTAAATGTC ACAACCAAAAATGCCGCCTTCGCAGTGGACATCTCTGATCAAGAAACCAGTACAGCCCTTGCTGCAGTAATGGGG TCTATGTTTGCCGTCATTAGCCTTGCGTCCATTGCTGTGTACTTTGCCAAAAGATTTAAGAGAAAAAACTACCAC CACTCATTAAAAAGTATATGCAAAAAACCTCTTCAATCCCACTAAATGAGCTGTACCCACCACTCATTAACCTC TGGGAAGGTGACAGCGAGAAAGACAAAGATGGTTCTGCAGACACCAAGCCAACCCAGGTCGACACACCAGAAGC ${\tt TATTACATGTGG} \underline{\textbf{TAA}} \textbf{CTCAGAGGATATTTTGCTTCTGGTAGTAAGGAGCACAAAGACGTTTTTGCTTTATTCTGC}$ AAAAGTGAACAAGTTGAAGACTTTTGTATTTTTGACTTTGCTAGTTTGTGGCAGAGTGGAGAGGGCGGGTGGATA TTTCAAATTTTTTTAGTATAGCGTATCGCAAGGGTTTGACACGGCTGCCAGCGACTCTAGGCTTCCAGTCTGTGT

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FIGURE 512

MARMSFVIAACQLVLGLLMTSLTESSIQNSECPQLCVCEIRPWFTPQSTYREATTVDCNDLRL
TRIPSNLSSDTQVLLLQSNNIAKTVDELQQLFNLTELDFSQNNFTNIKEVGLANLTQLTTLHL
EENQITEMTDYCLQDLSNLQELYINHNQISTISAHAFAGLKNLLRLHLNSNKLKVIDSRWFDS
TPNLEILMIGENPVIGILDMNFKPLANLRSLVLAGMYLTDIPGNALVGLDSLESLSFYDNKLV
KVPQLALQKVPNLKFLDLNKNPIHKIQEGDFKNMLRLKELGINNMGELVSVDRYALDNLPELT
KLEATNNPKLSYIHRLAFRSVPALESLMLNNNALNAIYQKTVESLPNLREISIHSNPLRCDCV
IHWINSNKTNIRFMEPLSMFCAMPPEYKGHQVKEVLIQDSSEQCLPMISHDSFPNRLNVDIGT
TVFLDCRAMAEPEPEIYWVTPIGNKITVETLSDKYKLSSEGTLEISNIQIEDSGRYTCVAQNV
QGADTRVATIKVNGTLLDGTQVLKIYVKQTESHSILVSWKVNSNVMTSNLKWSSATMKIDNPH
ITYTARVPVDVHEYNLTHLQPSTDYEVCLTVSNIHQQTQKSCVNVTTKNAAFAVDISDQETST
ALAAVMGSMFAVISLASIAVYFAKRFKRKNYHHSLKKYMQKTSSIPLNELYPPLINLWEGDSE
KDKDGSADTKPTQVDTSRSYYMW

Important features:

Signal peptide:

Amino acids 1-25

Transmembrane domain:

Amino acids 508-530

N-glycosylation sites:

Amino acids 69-73;96-100;106-110;117-121;385-389;517-521; 582-586;611-615

Tyrosine kinase phosphorylation site:

Amino acids 573-582

N-myristoylation sites:

Amino acids 16-22;224-230;464-470;637-643;698-704

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FIGURE 513

GGGAGAGAGGATAAATAGCAGCGTGGCTTCCCTGGCTCCTCTCTGCATCCTTCCCGACCTTCC CAGCAAT<u>ATG</u>CATCTTGCACGTCTGGTCGGCTCCTGCTCCTTCTGCTACTGGGGGCCCT GTCTGGATGGCCGCCAGCGATGACCCCATTGAGAAGGTCATTGAAGGGATCAACCGAGGGCT GAGCAATGCAGAGAGAGGGTGGGCAAGGCCCTGGATGGCATCAACAGTGGAATCACGCATGC CGGAAGGGAAGTGGAGAAGGTTTTCAACGGACTTAGCAACATGGGGAGCCACACCGGCAAGGA GTTGGACAAGGCGTCCAGGGGCTCAACCACGGCATGGACAAGGTTGCCCATGAGATCAACCA TGGTATTGGACAAGCAGGAAAGGAAGCAGAAGCTTGGCCATGGGGTCAACAACGCTGCTGG ACAGGCCGGGAAGGAAGCAGACAAAGCGGTCCAAGGGTTCCACACTGGGGTCCACCAGGCTGG GAAGGAAGCAGAGAAACTTGGCCAAGGGGTCAACCATGCTGCTGACCAGGCTGGAAAGGAAGT GGAGAAGCTTGGCCAAGGTGCCCACCATGCTGGCCAGGCCGGGAAGGAGCTGCAGAATGC TCATAATGGGGTCAACCAAGCCAGCAAGGAGGCCAACCAGCTGCTGAATGGCAACCATCAAAG CGGATCTTCCAGCCATCAAGGAGGGCCACAACCACGCCGTTAGCCTCTGGGGCCTCAGTCAA CACGCCTTTCATCAACCTTCCCGCCCTGTGGAGGAGCGTCGCCAACATCATGCCC**TAA**ACTGG CATCCGGCCTTGCTGGGAGAATAATGTCGCCGTTGTCACATCAGCTGACATGACCTGGAGGGG TTGGGGGTGGGGGACAGGTTTCTGAAATCCCTGAAGGGGGTTGTACTGGGATTTGTGAATAAA CTTGATACACCA

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FIGURE 514

MHLARLVGSCSLLLLLGALSGWAASDDPIEKVIEGINRGLSNAEREVGKALDGINSGITHAGR EVEKVFNGLSNMGSHTGKELDKGVQGLNHGMDKVAHEINHGIGQAGKEAEKLGHGVNNAAGQA GKEADKAVQGFHTGVHQAGKEAEKLGQGVNHAADQAGKEVEKLGQGAHHAAGQAGKELQNAHN GVNQASKEANQLLNGNHQSGSSSHQGGATTTPLASGASVNTPFINLPALWRSVANIMP

Important features:

Signal peptide:

amino acids 1-25

Homologous region to circumsporozoite (CS) repeats:

amino acids 35-225

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FIGURE 515

TTCCCTCCGACGCCCACGCTGCCCAGACATTCCGGCTGCCGGGTCTGGAGAGCTCCCCGAA CCCCTCCGCGGAGAGGAGCGAGGCGCGCCAGGGTGGCCCCCGGGGCGCGCTTGGTCTCGGAG AAGCGGGGACGAGGCCGGAGGATGAGCGACTGAGGGCGACGCGGGCACTGACGCGAGTTGGGG CCGCGACTACCGGCAGCTGACAGCGCGATGAGCGACTCCCCAGAGACGCCCTAGCCCGGTGTG CGCGCCAGGCGGAGCGCGCAGGTGGGGCTGTTAGTGGTCCGCCCCACGCGGGTCGCCG GCCGGCCCAGGATGGGCGCTGGCAACCCGGGCCCGCCGCCGCTGCTACCCCTGCGCCCGC TGCGAGCCCGGCGTCCGGCCCTGCGCTCATGGACGGCGGCTCCCGGCTGGCGGCGGC GACGTGGTAGGGG**ATG**CCCAGCTCCACTGCGATGGCAGTTGGCGCGCTCTCCAGTTCCCTCCT GGTCACCTGCTGCTGGTGGTCTGTGCAGTCCGAGCATCCCGCTGGAGAAGCTGGCCCA GGCACCAGAGCAGCCGGCCAGGAGAAGCGTGAGCACGCCACTCGGGACGGCCCGGGGCGGGT GAACGAGCTCGGGCGCCCGGCGAGGGACGAGGGCCGGCAGCGGCCGGGACTGGAAGAGCAAGAG CGGCCGTGGGCTCGCCGTGAGCCGTGGAGCAAGCTGAAGCAGGCCTGGGTCTCCCAGGG CGGGGGCCCAAGGCCGGGGATCTGCAGGTCCGGCCCCGCGGGGACACCCCGCAGGCGGAAGC CCTGGCCGCAGCCCCAGGACGCGATTGGCCCGGAACTCGCGCCCCACGCCCGAGCCACCCGA GGAGTACGTGTACCCGGACTACCGTGGCAAGGGCTGCGTGGACGAGAGCGGCTTCGTGTACGC GATCGGGGAGAAGTTCGCGCCGGGCCCTCGGCCTGCCCGTGCCTGTGCACCGAGGAGGGGCC GCTGTGCGCGCAGCCCGAGTGCCCGAGGCTGCACCCGCGCTGCATCCACGTCGACACGAGCCA GTGCTGCCGCAGTGCAAGGAGAGAAGAACTACTGCGAGTTCCGGGGCAAGACCTATCAGAC TTTGGAGGAGTTCGTGGTGTCTCCATGCGAGAGGTGTCGCTGTGAAGCCAACGGTGAGGTGCT ATGCACAGTGTCAGCGTGTCCCCAGACGGAGTGTGTGGACCCTGTGTACGAGCCTGATCAGTG CTGTCCCATCTGCAAAAATGGTCCAAACTGCTTTGCAGAAACCGCGGTGATCCCTGCTGGCAG AGAAGTGAAGACTGACGAGTGCACCATATGCCACTGTACTTATGAGGAAGGCACATGGAGAAT CGAGCGGCAGGCCATGTGCACGAGACATGAATGCAGGCAAATGTAGACGCTTCCCAGAACACA AACTCTGACTTTTCTAGAACATTTTACTGATGTGAACATTCTAGATGACTCTGGGAACTATC AGTCAAAGAAGACTTTTGATGAGGAATAATGGAAAATTGTTGGTACTTTTCCTTTTCTTGATA ACAGTTACTACAACAGAAGGAAATGGATATATTTCAAAACATCAACAAGAACTTTGGGCATAA CAAATGTATTTCTATAATCCCTCCATTAGAGAGCTTATATAAGTGTTTTCTATAGATGCAGAT

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FIGURE 516

MPSSTAMAVGALSSSLLVTCCLMVALCSPSIPLEKLAQAPEQPGQEKREHATRDGPGRVNELG RPARDEGGSGRDWKSKSGRGLAGREPWSKLKQAWVSQGGGAKAGDLQVRPRGDTPQAEALAAA AQDAIGPELAPTPEPPEEYVYPDYRGKGCVDESGFVYAIGEKFAPGPSACPCLCTEEGPLCAQ PECPRLHPRCIHVDTSQCCPQCKERKNYCEFRGKTYQTLEEFVVSPCERCRCEANGEVLCTVS ACPQTECVDPVYEPDQCCPICKNGPNCFAETAVIPAGREVKTDECTICHCTYEEGTWRIERQA MCTRHECRQM

Important features:

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 11-30

Glycosaminoglycan attachment site.

amino acids 80-83

N-myristoylation sites.

amino acids 10-15, 102-107, 103-108

Cell attachment sequence.

amino acids 114-117

EGF-like domain cysteine pattern signature.

amino acids 176-187

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FIGURE 517

GGACAACCGTTGCTGGGTGTCCCAGGGCCTGAGGCAGGACGGTACTCCGCTGACACCTTCCCT TTCGGCCTTGAGGTTCCCAGCCTGGTGGCCCCAGGACGTTCCGGTCGCATGGCAGAGTGCTAC GGACGACGCCT**ATG**AAGCCCTTAGTCCTTCTAGTTGCGCTTTTGCTATGGCCTTCGTCTGTGC CGGCTTATCCGAGCATAACTGTGACACCTGATGAAGAGCAAAACTTGAATCATTATATACAAG TTTTAGAGAACCTAGTACGAAGTGTTCCCTCTGGGGAGCCAGGTCGTGAGAAAAAATCTAACT CTCCAAAACATGTTTATTCTATAGCATCAAAGGGATCAAAATTTAAGGAGCTAGTTACACATG GAGACGCTTCAACTGAGAATGATGTTTTAACCAATCCTATCAGTGAAGAAACTACAACTTTCC CTACAGGAGGCTTCACACCGGAAATAGGAAAGAAAAAACACACGGAAAGTACCCCATTCTGGT CGATCAAACCAAACAATGTTTCCATTGTTTTGCATGCAGAGGAACCTTATATTGAAAATGAAG AGCCAGAGCCAGAGCCGGAGCCAGCTGCAAAACAAACTGAGGCACCAAGAATGTTGCCAGTTG TTACTGAATCATCTACAAGTCCATATGTTACCTCATACAAGTCACCTGTCACCACTTTAGATA AGAGCACTGGCATTGAGATCTCTACAGAATCAGAAGATGTTCCTCAGCTCTCAGGTGAAACTG CGATAGAAAAACCCGAAGAGTTTGGAAAGCACCCAGAGAGTTGGAATAATGATGACATTTTGA AAAAATTTTAGATATTAATTCACAAGTGCAACAGGCACTTCTTAGTGACACCAGCAACCCAG CATATAGAGAAGATATTGAAGCCTCTAAAGATCACCTAAAACGAAGCCTTGCTCTAGCAGCAG CAGCAGAACATAAATTAAAAACAATGTATAAGTCCCAGTTATTGCCAGTAGGACGAACAAGTA ATAAAATTGATGACATCGAAACTGTTATTAACATGCTGTGTAATTCTAGATCTAAACTCTATG AATATTTAGATATTAAATGTGTTCCACCAGAGATGAGAAAAAGCTGCTACAGTATTCAATA CATTAAAAAATATGTGTAGATCAAGGAGAGTCACAGCCTTATTAAAAGTTTAT**TAA**ACAATAA TATAAAAATTTTAAACCTACTTGATATTCCATAACAAAGCTGATTTAAGCAAACTGCATTTTT TCACAGGAGAAATAATCATATTCGTAATTTCAAAAGTTGTATAAAAATATTTTCTATTGTAGT TCAAATGTGCCAACATCTTTATGTGTCATGTGTTATGAACAATTTTCATATGCACTAAAAACC TAATTTAAAATAAAATTTTGGTTCAGGAAAAA

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FIGURE 518

MKPLVLLVALLLWPSSVPAYPSITVTPDEEQNLNHYIQVLENLVRSVPSGEPGREKKSNSPKH
VYSIASKGSKFKELVTHGDASTENDVLTNPISEETTTFPTGGFTPEIGKKKHTESTPFWSIKP
NNVSIVLHAEEPYIENEEPEPEPEPAAKQTEAPRMLPVVTESSTSPYVTSYKSPVTTLDKSTG
IEISTESEDVPQLSGETAIEKPEEFGKHPESWNNDDILKKILDINSQVQQALLSDTSNPAYRE
DIEASKDHLKRSLALAAAAEHKLKTMYKSQLLPVGRTSNKIDDIETVINMLCNSRSKLYEYLD
IKCVPPEMREKAATVFNTLKNMCRSRRVTALLKVY

Important features:

Signal peptide:

amino acids 1-19

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FIGURE 519

CGGCTCGAGTGCAGCTGTGGGGAGATTTCAGTGCATTGCCTCCCTGGGTGCTCTTCATCTTG GATTTGAAAGTTGAGAGCAGC**ATG**TTTTGCCCACTGAAACTCATCCTGCCAGTGTTACTG GATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTGGGT GATTCAGCTCTGATGGGATGTTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGATAGAC TGGACTCTGTCACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCAATCTC AGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGCAATGAT GGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGAAATCCGC CTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAGAGGAGCCC AAAGAGCTCATGGTCCATGTGGGTGGATTGATTCAGATGGGATGTGTTTTCCAGAGCACAGAA GTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGAGGAGATTGTA TTTCGTTACTACCACAAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGGGCCACTTCCAG AATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATGCTTCAAGGAGTG AGGGAGTCAGATGGAGGAAACTACACCTGCAGTATCCACCTAGGGAACCTGGTGTTCAAGAAA ACCATTGTGCTGCATGTCAGCCCGGAAGAGCCTCGAACACTGGTGACCCCGGCAGCCCTGAGG CCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTCTGTGCCACAATCCTG CTGCTCCCTGTTCTGATATTGATCGTGAAGAGACCTGTGGAAATAAGAGTTCAGTGAATTCT ACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAGAAAAACCCTGCCATTTT GAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTACGGGAGGTGATCGAGGAA GAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCACCCAGTTTGGCCTTCTCTG AGGTCAGATCGGAACAACTCACTTGAAAAAAAGTCAGGTGGGGGAATGCCAAAAACACAGCAA GTCCTGGGCCACTCTACCAGTGATTTCAGACTCCCGCTCTCCCAGCTGTCCTCCTGTCTCATT GTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGGCAGAGAGACTGGACAGCTCTGGA GGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGCCTCTGGAGTGGGACACTGGCCCTG GGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCCGTTGGATCAGACCCTCCTGTGGGCAGGG

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FIGURE 520

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPGE
HAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGESQV
FKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYYHKL
RMSVEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGNLVFKKTIVLHVS
PEEPRTLVTPAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKTCGNKSSVNSTVLVKNT
KKTNPEIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLRSDRNNS
LEKKSGGGMPKTQQAF

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FIGURE 521

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAATGTGTCCCATCTCACATGG TTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGGAA ACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCC**ATG**CAGGA TGAAGATGGATACATCACCTTAAATATTAAAACTCGGAAACCAGCTCTCGTCTCCGTTGGCCC TGCATCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGGATGGT TGTCGGGCTGGTGGCTCTGGGGATTTGGTCTGTCATGCAGCGCAATTACCTACAAGATGAGAA TGAAAATCGCACAGGAACTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGGTAAAACA ATCAGAACTAAAGGCCACTTTCAAAGGTCATAAATGCAGCCCCTGTGACACAAACTGGAGATA TTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAGAGAGTAAGCAGTA CTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGGAGTACATCAA AGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAATGAGGTCTGGAA GTGGGAGGTTGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGAAGATGGAAAAGGAAA TATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTGAGAACAACATTA TTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT**TAA**TGCAAAGAGGT GCTGAAAAAAAAAAAAA

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FIGURE 522

MQDEDGYITLNIKTRKPALVSVGPASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYLQ DENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYGDSCYGFFRHNLTWEES KQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEFLEDG KGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

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FIGURE 523

CAGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACC**ATG**GC AAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAAATCCAA GAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTTGGTATCCTGGCCCTAACTCTAAT TGTCCTGTTTTGGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGCCTATGACATGGA GCACACTTTCTACAGCAATGGAGAGAGAAGAAGATTTACATGGAAATTGATCCTGTGACCAG AACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGAAGTGCACGACTTTAAAAA CGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTTTATCAAAACTCAGATTAAAGT GATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGAGAATGAAGAAATTACCACAACTTT CTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAAGCCTATTGAAAACCGAGATTTTCTTAA AAATTCCAAAATTCTGGAGATTTGTGATAACGTGACCATGTATTGGATCAATCCCACTCTAAT ATCAGTTTCTGAGTTACAAGACTTTGAGGAGGAGGAGAAGATCTTCACTTTCCTGCCAACGA AAAAAAAGGGATTGAACAAAATGAACAGTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCG TCACGCCAGACAAGCAAGTGAGGAAGAACTTCCAATAAATGACTATACTGAAAATGGAATAGA ATTTGATCCCATGCTGGATGAGAGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTA TTGCCGCCGCGTCTGTGAACCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGG CAATGAATTTCTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCTCTCCAGAATTACTTGTAG

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FIGURE 524

MAKNPPENCEDCHILNAEAFKSKKICKSLKICGLVFGILALTLIVLFWGSKHFWPEVPKKAYD MEHTFYSNGEKKKIYMEIDPVTRTEIFRSGNGTDETLEVHDFKNGYTGIYFVGLQKCFIKTQI KVIPEFSEPEEEIDENEEITTTFFEQSVIWVPAEKPIENRDFLKNSKILEICDNVTMYWINPT LISVSELQDFEEEGEDLHFPANEKKGIEQNEQWVVPQVKVEKTRHARQASEEELPINDYTENG IEFDPMLDERGYCCIYCRRGNRYCRRVCEPLLGYYPYPYCYQGGRVICRVIMPCNWWVARMLGRV

Important features:

Signal peptide:

amino acids 1-40

Transmembrane domain:

amino acids 25-47 (type II)

N-glycosylation sites.

amino acids 94-97, 180-183

Glycosaminoglycan attachment sites.

amino acids 92-95, 70-73, 85-88, 133-136, 148-151, 192-195, 239-242

N-myristoylation sites.

amino acids 33-38, 95-100, 116-121, 215-220, 272-277

Microbodies C-terminal targeting signal.

amino acids 315-317

Cytochrome c family heme-binding site signature.

amino acids 9-14

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FIGURE 525

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FIGURE 526

MKITGGLLLLCTVVYFCSSSEAASLSPKKVDCSIYKKYPVVAIPCPITYLPVCGSDYITYGNE CHLCTESLKSNGRVQFLHDGSC

Important features:

Signal peptide:

amino acids 1-19

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FIGURE 527

CGACGATGCTACGCGCCCCGGCTGCCTCCTCCGGACCTCCGTAGCGCCTGCCGCGCCCTGG CTGCGGCGCTGCTCGTCGCTTGCGCGCTGCTCTCTTCTAGAGCCGAGGGACCCGGTGGCCT CGTCGCTCAGCCCCTATTTCGGCACCAAGACTCGCTACGAGGATGTCAACCCCGTGCTATTGT CGGGCCCCGAGGCTCCGTGGCGGGACCCTGAGCTGCTGGAGGGGGACCTGCACCCCGGTGCAGC TGGTCGCCCTCATTCGCCACGGCACCCGCTACCCCACGGTCAAACAGATCCGCAAGCTGAGGC AGCTGCACGGGTTGCTGCAGGCCCGCGGGTCCAGGGATGGCGGGGCTAGTAGTACCGGCAGCC TAGTAGAGAGGGACGCAGGATATGCGACAGCTGGCGCTGCGTCTGGCCTCGCTCTTCCCGG CCCTTTTCAGCCGTGAGAACTACGGCCGCCTGCGGCTCATCACCAGTTCCAAGCACCGCTGCA TGGATAGCAGCGCCGCCTTCCTGCAGGGGCTGTGGCAGCACTACCACCCTGGCTTGCCGCCGC CGGACGTCGCAGATATGGAGTTTGGACCTCCAACAGTTAATGATAAACTAATGAGATTTTTTTG ATCACTGTGAGAAGTTTTTAACTGAAGTAGAAAAAAATGCTACAGCTCTTTATCACGTGGAAG CAGTAAATGATTTAAATGCAGATTTAATTCAAGTAGCCTTTTTCACCTGTTCATTTGACCTGG CAATTAAAGGTGTTAAATCTCCTTGGTGTGTGTTTTTTGACATAGATGATGCAAAGGTATTAG AATATTTAAATGATCTGAAACAATATTGGAAAAGAGGATATGGGTATACTATTAACAGTCGAT CCAGCTGCACCTTGTTTCAGGATATCTTTCAGCACTTGGACAAAGCAGTTGAACAGAAACAAA GGTCTCAGCCAATTTCTTCTCCAGTCATCCTCCAGTTTGGTCATGCAGAGACTCTTCTTCCAC TGCTTTCTCATGGGCTACTTCAAAGACAAGGAACCCCTAACAGCGTACAATTACAAAAAAAC AAATGCATCGGAAGTTCCGAAGTGGTCTCATTGTACCTTATGCCTCGAACCTGATATTTGTGC TTTACCACTGTGAAAATGCTAAGACTCCTAAAGAACAATTCCGAGTGCAGATGTTATTAAATG AAAAGGTGTTACCTTTGGCTTACTCACAAGAAACTGTTTCATTTTATGAAGATCTGAAGAACC ACTACAAGGACATCCTTCAGAGTTGTCAAACCAGTGAAGAATGTGAATTAGCAAGGGCTAACA GTACATCTGATGAACTA**TGA**GTAACTGAAGAACATTTTTAATTCTTTAGGAATCTGCAATGAG TGATTACATGCTTGTAATAGGTAGGCAATTCCTTGATTACAGGAAGCTTTTATATTACTTGAG TATTTCTGTCTTTTCACAGAAAAACATTGGGTTTCTCTCTGGGTTTTGGACATGAAATGTAAGA AAAGATTTTTCACTGGAGCAGCTCTCTTAAGGAGAAACAAATCTATTTAGAGAAACAGCTGGC CCTGCAAATGTTTACAGAAATGAAATTCTTCCTACTTATATAAGAAATCTCACACTGAGATAG AATTGTGATTTCATAATAACACTTGAAAAGTGCTGGAGTAACAAAATATCTCAGTTGGACCAT CCTTAACTTGATTGAACTGTCTAGGAACTTTACAGATTGTTCTGCAGTTCTCTCTTCTTTTCC TCAGGTAGGACAGCTCTAGCATTTTCTTAATCAGGAATATTGTGGTAAGCTGGGAGTATCACT CTGGAAGAAGTAACATCTCCAGATGAGAATTTGAAACAAGAAACAGAGTGTTGTAAAAGGAC ATATTTGAACATTTTTTCAATAATTCCTTTTTACTTCTAGGAAGTCTCAAAAGACCATCTTAA ATTATTATATGTTTGGACAATTAGCAACAAGTCAGATAGTTAGAATCGAAGTTTTTCAAATCC ATTGCTTAGCTAACTTTTTCATTCTGTCACTTGGCTTCGATTTTTATATTTTCCTATTATATG

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FIGURE 528

MLRAPGCLLRTSVAPAAALAAALLSSLARCSLLEPRDPVASSLSPYFGTKTRYEDVNPVLLSG
PEAPWRDPELLEGTCTPVQLVALIRHGTRYPTVKQIRKLRQLHGLLQARGSRDGGASSTGSRD
LGAALADWPLWYADWMDGQLVEKGRQDMRQLALRLASLFPALFSRENYGRLRLITSSKHRCMD
SSAAFLQGLWQHYHPGLPPPDVADMEFGPPTVNDKLMRFFDHCEKFLTEVEKNATALYHVEAF
KTGPEMQNILKKVAATLQVPVNDLNADLIQVAFFTCSFDLAIKGVKSPWCDVFDIDDAKVLEY
LNDLKQYWKRGYGYTINSRSSCTLFQDIFQHLDKAVEQKQRSQPISSPVILQFGHAETLLPLL
SLMGYFKDKEPLTAYNYKKQMHRKFRSGLIVPYASNLIFVLYHCENAKTPKEQFRVQMLLNEK
VLPLAYSQETVSFYEDLKNHYKDILQSCQTSEECELARANSTSDEL

Important features:

Signal sequence

amino acids 1-30

N-glycosylation sites.

amino acids 242-246, 481-485

N-myristoylation sites.

amino acids 107-113, 113-119, 117-123, 118-124, 128-134

Endoplasmic reticulum targeting sequence.

amino acids 484-489

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FIGURE 529

GGAGAGCCGCGGCTGGGACCGGAGTGGGGAGCGCGCGTGGAGGTGCCACCCGGCGCGGGTGG CGGAGAGATCAGAAGCCTCTTCCCCAAGCCGAGCCAACCTCAGCGGGGACCCGGGCTCAGGGA CGCGGCGGCGGCGGCGACTGCAGTGGCTGGACGATGGCAGCGTCCGCCGGAGCCGGGGCG TTGACAGCTGGAGTATCAGCCTTGGAAGTATATACGCCAAAAGAAATCTTCGTGGCAAATGGT ACACAAGGGAAGCTGACCTGCAAGTTCAAGTCTACTAGTACGACTGGCGGGTTGACCTCAGTC TCCTGGAGCTTCCAGCCAGAGGGGCCGACACTACTGTGTCGTTTTTCCACTACTCCCAAGGG CAAGTGTACCTTGGGAATTATCCACCATTTAAAGACAGAATCAGCTGGGCTGGAGACCTTGAC AAGAAAGATGCATCAATCAACATAGAAAATATGCAGTTTATACACAATGGCACCTATATCTGT GATGTCAAAAACCCTCCTGACATCGTTGTCCAGCCTGGACACATTAGGCTCTATGTCGTAGAA AAAGAGAATTTGCCTGTGTTTCCAGTTTGGGTAGTGGTGGGCATAGTTACTGCTGTGGTCCTA GGTCTCACTCTGCTCATCAGCATGATTCTGGCTGTCCTCTATAGAAGGAAAAACTCTAAACGG GATTACACTGGCTGCAGTACATCAGAGAGTTTGTCACCAGTTAAGCAGGCTCCTCGGAAGTCC CCCTCCGACACTGAGGGTCTTGTAAAGAGTCTGCCTTCTGGATCTCACCAGGGCCCAGTCATA TATGCACAGTTAGACCACTCCGGCGGACATCACAGTGACAAGATTAACAAGTCAGAGTCTGTG GTGTATGCGGATATCCGAAAGAAT**TAA**GAGAATACCTAGAACATATCCTCAGCAAGAAACAAA ACCAAACTGGACTCTCGTGCAGAAAATGTAGCCCATTACCACATGTAGCCTTGGAGACCCAGG CAAGGACAAGTACACGTGTACTCACAGAGGGAGAGAAAGATGTGTACAAAGGATATGTATAAA TATTCTATTTAGTCATCCTGATATGAGGAGCCAGTGTTGCATGATGAAAAGATGGTATGATTC ATTTCAGAAACATTCCTTTCACCATCATTTAGAAATGGTTTGCCTTAATGGAGACAATAGCAG ATCCTGTAGTATTTCCAGTAGACATGGCCTTTTAATCTAAGGGCTTAAGACTGATTAGTCTTA GCATTTACTGTAGTTGGAGGATGGAGATGCTATGATGGAAGCATACCCAGGGTGGCCTTTAGC ACAGTATCAGTACCATTTATTTGTCTGCCGCTTTTAAAAAATACCCATTGGCTATGCCACTTG AAAACAATTTGAGAAGTTTTTTTGAAGTTTTTCTCACTAAAATATGGGGCAATTGTTAGCCTT ACATGTTGTGTAGACTTACTTTAAGTTTGCACCCTTGAAATGTGTCATATCAATTTCTGGATT CATAATAGCAAGATTAGCAAAGGATAAATGCCGAAGGTCACTTCATTCTGGACACAGTTGGAT CAATACTGATTAAGTAGAAAATCCAAGCTTTGCTTGAGAACTTTTGTAACGTGGAGAGTAAAA AGTATCGGTTTTA

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FIGURE 530

MAASAGAGAVIAAPDSRRWLWSVLAAALGLLTAGVSALEVYTPKEIFVANGTQGKLTCKFKST STTGGLTSVSWSFQPEGADTTVSFFHYSQGQVYLGNYPPFKDRISWAGDLDKKDASINIENMQ FIHNGTYICDVKNPPDIVVQPGHIRLYVVEKENLPVFPVWVVVGIVTAVVLGLTLLISMILAV LYRRKNSKRDYTGCSTSESLSPVKQAPRKSPSDTEGLVKSLPSGSHQGPVIYAQLDHSGGHHS DKINKSESVVYADIRKN

Important features:

Signal peptide:

amino acids 1-37

Transmembrane domain:

amino acids 161-183

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FIGURE 531

GGCTGGTGGGAAGAGCCGAG**ATG**GCGGCAGCCAGCGCTGGGGCAACCCGGCTGCTCCTGCTC TTGCTGATGGCGGTAGCAGCGCCCAGTCGAGCCCGGGGCAGCGGCTGCCGGGCCGGGACTGGT GCGCGAGGGCTGGGGCGGAAGGTCGAGAGGCCGAGGCCTGTGGCACGGTGGGGCTGCTGCTG GAGCACTCATTTGAGATCGATGACAGTGCCAACTTCCGGAAGCGGGGCTCACTGCTCTGGAAC CAGCAGGATGGTACCTTGTCCCTGTCACAGCGGCAGCTCAGCGAGGAGGAGCGGGGCCGACTC CGGGATGTGGCAGCCCTGAATGGCCTGTACCGGGTCCGGATCCCAAGGCGACCCGGGGCCCTG GATGGCCTGGAAGCTGGTGGCTATGTCTCCTCCTTTGTCCCTGCGTGCTCCCTGGTGGAGTCG CACCTGTCGGACCACGTGCACGTGGATGTGGCCGCAACGTGGTGGGCGTGTCGGTG GTGACGCACCCCGGGGCCTGCCGGGGCCATGAGGTGGAGGTGGACCTGGAGCTGTTCAAC ACCTCGGTGCAGCTGCAGCCCCACCACAGCCCCAGGCCCTGAGACGGCGGCCTTCATTGAG CGCCTGGAGATGGAACAGGCCCAGAAGGCCAAGAACCCCCAGGAGCAGAAGTCCTTCTTCGCC AAATACTGGATGTACATCATTCCCGTCGTCCTGTTCCTCATGATGTCAGGAGCGCCAGACACC GGGGGCCAGGGTGGGGGTGGGGGTGGTGGTGGGGGTAGTGGCCTTTGCTGTGTGCCA CCCTCCCTGTAAGTCTATTTAAAAACATCGACGATACATTGAAATGTGTGAACGTTTTGAAAA GCTACAGCTTCCAGCAGCCAAAAGCAACTGTTGTTTTGGCAAGACGGTCCTGATGTACAAGCT TGATTGAAATTCACTGCTCACTTGATACGTTATTCAGAAACCCAAGGAATGGCTGTCCCCATC CTCATGTGGCTGTGTGGAGCTCAGCTGTGTTGTGTGGCAGTTTATTAAACTGTCCCCCAGATC GACACGCAAAAAAAAA

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FIGURE 532

MAAASAGATRLLLLLLMAVAAPSRARGSGCRAGTGARGAGAEGREGEACGTVGLLLEHSFEID DSANFRKRGSLLWNQQDGTLSLSQRQLSEEERGRLRDVAALNGLYRVRIPRRPGALDGLEAGG YVSSFVPACSLVESHLSDQLTLHVDVAGNVVGVSVVTHPGGCRGHEVEDVDLELFNTSVQLQP PTTAPGPETAAFIERLEMEQAQKAKNPQEQKSFFAKYWMYIIPVVLFLMMSGAPDTGGQGGG GGGGGGGGGGCCCVPPSL

Important features:

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 226-243

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FIGURE 533

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FIGURE 534

MELALLCGLVVMAGVIPIQGGILNLNKMVKQVTGKMPILSYWPYGCHCGLGGRGQPKDATDWC CQTHDCCYDHLKTQGCGIYKDNNKSSIHCMDLSQRYCLMAVFNVIYLENEDSE

Important features:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 1-24

N-glycosylation site.

amino acids 86-89

N-myristoylation sites.

amino acids 20-25, 45-50

Phospholipase A2 histidine active site.

amino acids 63-70

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FIGURE 535

GCTGAGCGTGTGCGCGGTACGGGGCTCTCCTGCCTTCTGGGCTCCAACGCAGCTCTGTGGCTG AACTGGGTGCTCATCACGGGAACTGCTGGGCTATGGAATACAGATGTGGCAGCTCAGGTAGCC CCAAATTGCCTGGAAGAATACATCATGTTTTTCGATAAGAAGAAATTGTAGGATCCAGTTTTT TTTTTAACCGCCCCCCCCCCCCCCCCAAAAAAACTGTAAAGATGCAAAAACGTAATATCCAT GTTCTTGGAGTGTTCTGCGTGGCTGGCAAAGAATAATGTTCCAAAATCGGTCCATCTCCCAAG GGGTCCAATTTTCCTCCTGGGTGTCAGCGAGCCCTGACTCACTACAGTGCAGCTGACAGGGG CTGTCATGCAACTGGCCCCTAAGCCAAAGCAAAAGACCTAAGGACGACCTTTGAACAATACAA AGG<u>ATG</u>GGTTTCAATGTAATTAGGCTACTGAGCGGATCAGCTGTAGCACTGGTTATAGCCCCC ACTGTCTTACTGACAATGCTTTCTTCTGCCGAACGAGGATGCCCTAAGGGCTGTAGGTGTGAA GGCAAAATGGTATATTGTGAATCTCAGAAATTACAGGAGATACCCTCAAGTATATCTGCTGGT TGCTTAGGTTTGTCCCTTCGCTATAACAGCCTTCAAAAACTTAAGTATAATCAATTTAAAGGG CTCAACCAGCTCACCTGGCTATACCTTGACCATAACCATATCAGCAATATTGACGAAAATGCT TTTAATGGAATACGCAGACTCAAAGAGCTGATTCTTAGTTCCAATAGAATCTCCTATTTTCTT AACAATACCTTCAGACCTGTGACAAATTTACGGAACTTGGATCTGTCCTATAATCAGCTGCAT TCTCTGGGATCTGAACAGTTTCGGGGCTTGCGGAAGCTGCTGAGTTTACATTTACGGTCTAAC TCCCTGAGAACCATCCCTGTGCGAATATTCCAAGACTGCCGCAACCTGGAACTTTTGGACCTG GGATATAACCGGATCCGAAGTTTAGCCAGGAATGTCTTTGCTGGCATGATCAGACTCAAAGAA CTTCACCTGGAGCACAATCAATTTTCCAAGCTCAACCTGGCCCTTTTTCCAAGGTTGGTCAGC CTTCAGAACCTTTACTTGCAGTGGAATAAAATCAGTGTCATAGGACAGACCATGTCCTGGACC TGGAGCTCCTTACAAAGGCTTGATTTATCAGGCAATGAGATCGAAGCTTTCAGTGGACCCAGT GTTTTCCAGTGTGTCCCGAATCTGCAGCGCCTCAACCTGGATTCCAACAAGCTCACATTTATT GGTCAAGAGATTTTGGATTCTTGGATATCCCTCAATGACATCAGTCTTGCTGGGAATATATGG GAATGCAGCAGAAATATTTGCTCCCTTGTAAACTGGCTGAAAAGTTTTAAAGGTCTAAGGGAG AATACAATTATCTGTGCCAGTCCCAAAGAGCTGCAAGGAGTAAATGTGATCGATGCAGTGAAG AACTACAGCATCTGTGGCAAAAGTACTACAGAGAGGTTTGATCTGGCCAGGGCTCTCCCAAAG CCGACGTTTAAGCCCAAGCTCCCCAGGCCGAAGCATGAGAGCAAACCCCCTTTGCCCCCGACG GTGGGAGCCACAGAGCCCGGCCCAGAGACCGATGCTGACGCCGAGCACATCTCTTTCCATAAA ATCATCGCGGGCAGCGTGGCGCTTTTCCTGTCCGTGCTCATCCTGCTGGTTATCTACGTG TCATGGAAGCGGTACCCTGCGAGCATGAAGCAGCTGCAGCAGCGCTCCCTCATGCGAAGGCAC AGGAAAAAGAAAGACAGTCCCTAAAGCAAATGACTCCCAGCACCCAGGAATTTTATGTAGAT TATAAACCCACCAACACGGAGACCAGCGAGATGCTGCTGAATGGGACGGGACCCTGCACCTAT AACAAATCGGGCTCCAGGGAGTGTGAGGTA**TGA**ACCATTGTGATAAAAAGAGCTCTTAAAAGC TGGGAAATAAGTGGTGCTTTATTGAACTCTGGTGACTATCAAGGGAACGCGATGCCCCCCCTC GAAGCTTGAACTCCGGTTTAATATATACCTATTGTATAAGACCCTTTACTGATTCCATTAAT

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FIGURE 536

MGFNVIRLLSGSAVALVIAPTVLLTMLSSAERGCPKGCRCEGKMVYCESQKLQEIPSSISAGC LGLSLRYNSLQKLKYNQFKGLNQLTWLYLDHNHISNIDENAFNGIRRLKELILSSNRISYFLN NTFRPVTNLRNLDLSYNQLHSLGSEQFRGLRKLLSLHLRSNSLRTIPVRIFQDCRNLELLDLG YNRIRSLARNVFAGMIRLKELHLEHNQFSKLNLALFPRLVSLQNLYLQWNKISVIGQTMSWTW SSLQRLDLSGNEIEAFSGPSVFQCVPNLQRLNLDSNKLTFIGQEILDSWISLNDISLAGNIWE CSRNICSLVNWLKSFKGLRENTIICASPKELQGVNVIDAVKNYSICGKSTTERFDLARALPKP TFKPKLPRPKHESKPPLPPTVGATEPGPETDADAEHISFHKIIAGSVALFLSVLVILLVIYVS WKRYPASMKQLQQRSLMRRHRKKKRQSLKQMTPSTQEFYVDYKPTNTETSEMLLNGTGPCTYN KSGSRECEV

Important features:

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 420-442

N-glycosylation sites.

amino acids 126-129, 357-360, 496-499, 504-507

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 465-468

Tyrosine kinase phosphorylation site.

amino acids 136-142

N-myristoylation sites.

amino acids 11-16, 33-38, 245-250, 332-337, 497-502, 507-512

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FIGURE 537

GGGACTACAAGCCGCGCCGCCGCCGCCGCCCCCCCAGCAACCCTCGACATCGCGCTGAGGCGGCCACCGCGAC TCCGGCTCTGCGCTGCCTGACTTCTTCCTGCTGCTGCTTTTCAGGGGCTGCCTGATAGGGGCTGTAAATC TCAAATCCAGCAATCGAACCCCAGTGGTACAGGAATTTGAAAGTGTGGAACTGTCTTGCATCATTACGGATTCGC AGACAAGTGACCCCAGGATCGAGTGGAAGAAAATTCAAGATGAACAAACCACATATGTGTTTTTTGACAACAAAA TTCAGGGAGACTTGGCGGGTCGTGCAGAAATACTGGGGAAGACATCCCTGAAGATCTGGAATGTGACACGGAGAG ACTCAGCCCTTTATCGCTGTGAGGTCGTTGCTCGAAATGACCGCAAGGAAATTGATGAGATTGTGATCGAGTTAA CTGTGCAAGTGAAGCCAGTGACCCCTGTCTGTAGAGTGCCGAAGGCTGTACCAGTAGGCAAGATGGCAACACTGC ACTGCCAGGAGAGTGAGGGCCACCCCGGCCTCACTACAGCTGGTATCGCAATGATGTACCACTGCCCACGGATT TTCACAAGGACGACTCTGGGCAGTACTACTGCATTGCTTCCAATGACGCAGGCTCAGCCAGGTGTGAGGAGCAGG TCACGTTGGGCATCTGCTGTGCATACAGACGTGGCTACTTCATCAACAATAAACAGGATGGAGAAAGTTACAAGA TGATC<u>TGAGAGCCCGCGGTGTGGCTGAGAGCGCACAGAGCGCACGTGCACATACCTCTGCTAGAAACTCCTGTCAA</u> GGCAGCGAGAGCTGATGCACTCGGACAGAGCTAGACACTCATTCAGAAGCTTTTCGTTTTGGCCAAAGTTGACCA CTACTCTTCTTACTCTAACAAGCCACATGAATAGAAGAATTTTCCTCAAGATGGACCCGGTAAATATAACCACAA GGAAGCGAAACTGGGTGCGTTCACTGAGTTGGGTTCCTAATCTGTTTCTGGCCTGATTCCCGCATGAGTATTAGG ${\tt GTGATCTTAAAGAGTTTGCTCACGTAAACGCCCGTGCTGGGGCCCTGTGAAGCCAGCATGTTCACCACTGGTCGTT}$ CAGCAGCCACGACAGCATGTGAGATGGCGAGGTGGCTGGACAGCACCAGCAGCGCATCCCGGCGGAACCCA GAAAAGGCTTCTTACACAGCAGCCTTACTTCATCGGCCCACAGACACCACCGCAGTTTCTTCTTAAAGGCTCTGC TGATCGGTGTTGCAGTGTCCATTGTGGAGAAGCTTTTTGGATCAGCATTTTGTAAAAACAACCAAAATCAGGAAG GTAAATTGGTTGCTGGAAGAGGGATCTTGCCTGAGGAACCCTGCTTGTCCAACAGGGTGTCAGGATTTAAGGAAA ACCTTCGTCTTAGGCTAAGTCTGAAATGGTACTGAAATATGCTTTTCTATGGGTCTTGTTTATTTTATAAAATTT TACATCTAAATTTTTGCTAAGGATGTATTTTGATTATTGAAAAGAAAATTTCTATTTAAACTGTAAATATATTGT CATACAATGTTAAATAACCTATTTTTTTAAAAAAGTTCAACTTAAGGTAGAAGTTCCAAGCTACTAGTGTTAAAT TGGAAAATATCAATAATTAAGAGTATTTTACCCAAGGAATCCTCTCATGGAAGTTTACTGTGATGTTCCTTTTCT CACACAAGTTTTAGCCTTTTTCACAAGGGAACTCATACTGTCTACACATCAGACCATAGTTGCTTAGGAAACCTT TAAAAATTCCAGTTAAGCAATGTTGAAATCAGTTTGCATCTCTTCAAAAGAAACCTCTCAGGTTAGCTTTGAACT ${\tt CCAGTCAGCTCCTGGGGTTGCGCCAGGCGCCCCCGCTCTAGCTCACTGTTGCCTCGCTGTCTGCCAGGAGGCCCT}$ GCCATCCTTGGGCCCTGGCAGTGGCTGTCCCAGTGAGCTTTACTCACGTGGCCCTTGCTTCATCCAGCACAGC TCTCAGGTGGGCACTGCAGGGACACTGGTGTCTTCCATGTAGCGTCCCAGCTTTGGGCTCCTGTAACAGACCTCT AAGATTGTCTAAGGCCAAAGGCAATTGCGAAATCAAGTCTGTCAAGTACAATAACATTTTTAAAAGAAAATGGAT GGAGTGGCGGCCAGTCCAGCCTTTTAAAGAACGTCAGGTGGAGCAGCCAGGTGAAAGGCCTGGCGGGGAGGAAAG TGAAACGCCTGAATCAAAAGCAGTTTTCTAATTTTTGACTTTTAAATTTTTCATCCGCCGGAGACACTGCTCCCATT TGTGGGGGGACATTAGCAACATCACTCAGAAGCCTGTGTTCTTCAAGAGCAGGTGTTCTCAGCCTCACATGCCCT GCCGTGCTGGACTCAGGACTGAAGTGCTGTAAAGCAAGGAGCTGCTGAGAAGGAGCACTCCACTGTGTGCCTGGA **AATTGCATACATGAGACTGTGTTGACTTTTTTTAGTTATGTGAAACACTTTGCCGCAGGCCGCCTGGCAGAGGCA** GGAAATGCTCCAGCAGTGGCTCAGTGCTCCCTGGTGTCTGCTGCATGGCATCCTGGATGCTTAGCATGCAAGTTC CCTCCATCATTGCCACCTTGGTAGAGAGGGATGGCTCCCCACCCTCAGCGTTGGGGGATTCACGCTCCAGCCTCCT TCTTGGTTGTCATAGTGATAGGGTAGCCTTATTGCCCCCTCTTCTTATACCCTAAAACCTTCTACACTAGTGCCA TGGGAACCAGGTCTGAAAAAGTAGAGAGAGTGAAAGTAGAGTCTGGGAAGTAGCTGCCTATAACTGAGACTAGA CGGAAAAGGAATACTCGTGTATTTTAAGATATGAATGTGACTCAAGACTCGAGGCCGATACGAGGCTGTGATTCT GCCTTTGGATGGATGTTGCTGTACACAGATGCTACAGACTTGTACTAACACACCGTAATTTGGCATTTGTTTAAC CTCATTTATAAAAGCTTCAAAAAAACCCA

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FIGURE 538

MALRRPPRLRLCARLPDFFLLLLFRGCLIGAVNLKSSNRTPVVQEFESVELSCIITDSQTSDP RIEWKKIQDEQTTYVFFDNKIQGDLAGRAEILGKTSLKIWNVTRRDSALYRCEVVARNDRKEI DEIVIELTVQVKPVTPVCRVPKAVPVGKMATLHCQESEGHPRPHYSWYRNDVPLPTDSRANPR FRNSSFHLNSETGTLVFTAVHKDDSGQYYCIASNDAGSARCEEQEMEVYDLNIGGIIGGVLVV LAVLALITLGICCAYRRGYFINNKQDGESYKNPGKPDGVNYIRTDEEGDFRHKSSFVI

Important features:

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 243-263

N-glycosylation sites.

amino acids 104-107, 192-195

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 107-110

Casein kinase II phosphorylation site.

amino acids 106-109, 296-299

Tyrosine kinase phosphorylation site.

amino acids 69-77

N-myristoylation sites.

amino acids 26-31, 215-220, 226-231, 243-248, 244-249, 262-267

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FIGURE 539

CCAGGACCAGGGCGCACCGGCTCAGCCTCTCACTTGTCAGAGGCCGGGGAAGAAGCAAAGC GCAACGGTGTGGTCCAAGCCGGGGCTTCTGCTTCGCCTCTAGGACATACACGGGACCCCCTAA CTTCAGTCCCCCAAACGCGCACCCTCGAAGTCTTGAACTCCAGCCCCGCACATCCACGCGCGG CACAGGCGCGGCAGGCGGCGGCCGAAGGCGATGCGCGCAGGGGGTCGGGCAGCTGG GCTCGGGCGGGGGTAGGGCCCGGCAGGGAGGCAGGGAGGCTGCATATTCAGAGTCGCGGG CTGCGCCCTGGGCAGAGGCCGCCCTCGCTCCACGCAACACCTGCTGCTGCCACCGCGCCGCGA **TG**AGCCGCGTGGTCTCGCTGCTGCGGCGCCGCCGCTCTCTGCGCCCACGGAGCCTTCTGCC GCCGCGTGGTCAGCGGCCAAAAGGTGTGTTTTGCTGACTTCAAGCATCCCTGCTACAAAATGG CCTACTTCCATGAACTGTCCAGCCGAGTGAGCTTTCAGGAGGCACGCCTGGCTTGTGAGAGTG AGGGAGGAGTCCTCCTCAGCCTTGAGAATGAAGCAGAACAGAAGTTAATAGAGAGCATGTTGC AAAACCTGACAAAACCCGGGACAGGGATTTCTGATGGTGATTTCTGGATAGGGCTTTGGAGGA ATGGAGATGGGCAAACATCTGGTGCCTGCCCAGATCTCTACCAGTGGTCTGATGGAAGCAATT CCCAGTACCGAAACTGGTACACAGATGAACCTTCCTGCGGAAGTGAAAAGTGTGTTGTGATGT ATCACCAACCAACTGCCAATCCTGGCCTTGGGGGTCCCTACCTTTACCAGTGGAATGATGACA GGTGTAACATGAAGCACAATTATATTTGCAAGTATGAACCAGAGATTAATCCAACAGCCCCTG TAGAAAAGCCTTATCTTACAAATCAACCAGGAGACACCCATCAGAATGTGGTTGTTACTGAAG CAGGTATAATTCCCAATCTAATTTATGTTGTTATACCAACAATACCCCTGCTCTTACTGATAC TGGTTGCTTTTGGAACCTGTTGTTTCCAGATGCTGCATAAAAGTAAAGGAAGAACAAAAACTA **AA**TAACTCATTGACTTGGTTCCAGAATTTTGTAATTCTGGATCTGTATAAGGAATGGCATCAG AACAATAGCTTGGAATGGCTTGAAATCACAAAGGATCTGCAAGATGAACTGTAAGCTCCCCCT TGAGGCAAATATTAAAGTAATTTTTATATGTCTATTATTTCATTTAAAGAATATGCTGTGCTA ATAATGGAGTGAGACATGCTTATTTTGCTAAAGGATGCACCCAAACTTCAAACTTCAAGCAAA TGAAATGGACAATGCAGATAAAGTTGTTATCAACACGTCGGGAGTATGTGTGTTAGAAGCAAT TCCTTTTATTTCTTCACCTTTCATAAGTTGTTATCTAGTCAATGTAATGTATATTGTATTGA AATTTACAGTGTGCAAAAGTATTTTACCTTTGCATAAGTGTTTGATAAAAATGAACTGTTCTA ATATTTATTTTATGGCATCTCATTTTTCAATACATGCTCTTTTGATTAAAGAAACTTATTAC ATAATTCATCTTTCAGCTTCTCTGCTTTTGGTCAATGTCTAGGAAATCTCTTCAGAAATAAGA AGCTATTTCATTAAGTGTGATATAAACCTCCTCAAACATTTTACTTAGAGGCAAGGATTGTCT AATTTCAATTGTGCAAGACATGTGCCTTATAATTATTTTTTAGCTTAAAATTAAACAGATTTTG TAATAATGTAACTTTGTTAATAGGTGCATAAACACTAATGCAGTCAATTTGAACAAAAGAAGT GACATACACAATATAAATCATATGTCTTCACACGTTGCCTATATAATGAGAAGCAGCTCTCTG AGGGTTCTGAAATCAATGTGGTCCCTCTCTTGCCCACTAAACAAAGATGGTTGTTCGGGGTTT GGGATTGACACTGGAGGCAGATAGTTGCAAAGTTAGTCTAAGGTTTCCCTAGCTGTATTTAGC CTCTGACTATATTAGTATACAAAGAGGTCATGTGGTTGAGACCAGGTGAATAGTCACTATCAG TGTGGAGACAAGCACACACACACATTTTAGGAAGGAAAGGAACTACGAAATCGTGTGAAA ATGGGTTGGAACCCATCAGTGATCGCATATTCATTGATGAGGGTTTGCTTGAGATAGAAAATG GTGGCTCCTTTCTGTCTTATCTCCTAGTTTCTTCAATGCTTACGCCTTGTTCTTCTCAAGAGA AAGTTGTAACTCTCTGGTCTTCATATGTCCCTGTGCTCCTTTTAACCAAATAAAGAGTTCTTG

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FIGURE 540

MSRVVSLLLGAALLCGHGAFCRRVVSGQKVCFADFKHPCYKMAYFHELSSRVSFQEARLACES EGGVLLSLENEAEQKLIESMLQNLTKPGTGISDGDFWIGLWRNGDGQTSGACPDLYQWSDGSN SQYRNWYTDEPSCGSEKCVVMYHQPTANPGLGGPYLYQWNDDRCNMKHNYICKYEPEINPTAP VEKPYLTNQPGDTHQNVVVTEAGIIPNLIYVVIPTIPLLLLILVAFGTCCFQMLHKSKGRTKT SPNQSTLWISKSTRKESGMEV

Important features:

Signal peptide:

amino acids 1-21

Transmembrane domain:

amino acids 214-235

N-glycosylation sites.

amino acids 86-89 and 255-258

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 266-269

N-myristoylation sites.

amino acids 27-32, 66-71, 91-96, 93-98, 102-107, 109-114, 140-145 and 212-217

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FIGURE 541

CCACAGCCACTGGGCCCGAAGTTGCTCAGCCTGAAGTAGACACCACCCTGGGTCGTGTGCGAGGCCGGCAGGTGG GCGTGAAGGGCACAGACCGCCTTGTGAATGTCTTTCTGGGCATTCCATTTGCCCAGCCGCCACTGGGCCCTGACC GGTTCTCAGCCCCACACCCAGCACAGCCCTGGGAGGGTGTGCGGGATGCCAGCACTGCGCCCCCAATGTGCCTAC AAGACGTGGAGAGCATGAACAGCAGCAGATTTGTCCTCAACGGAAAACAGCAGATCTTCTCCGTTTCAGAGGACT GCCTGGTCCTCAACGTCTATAGCCCAGCTGAGGTCCCGCAGGGTCCGGTAGGCCGGTCATGGTATGGGTCCATG GAGGCGCTCTGATAACTGGCGCTGCCACCTCCTACGATGGATCAGCTCTGGCTGCCTATGGGGATGTGGTCGTGG TTACAGTCCAGTACCGCCTTGGGGTCCTTGGCTTCTTCAGCACTGGAGATGAGCATGCACCTGGCAACCAGGGCT TCCTAGATGTGGTAGCTGCTTTGCGCTGGGTGCAAGAAAACATCGCCCCCTTCGGGGGTGACCTCAACTGTGTCA CTGTCTTTGGTGGATCTGCCGGTGGGAGCATCATCTCTGGCCTGGTCCTGTCCCCAGTGGCTGCAGGGCTGTTCC ACAGAGCCATCACACAGAGTGGGGTCATCACCACCCCAGGGATCATCGACTCTCACCCTTGGCCCCTAGCTCAGA GCCCCAAGGAACTCCTGAAGGAGAAGCCCTTCCACTCTGTGCCCTTCCTCATGGGTGTCAACAACCATGAGTTCA GCTGGCTCATCCCCAGGGGCTGGGGTCTCCTGGATACAATGGAGCAGATGAGCCGGGAGGACATGCTGGCCATCT CAACACCCGTCTTGACCAGTCTGGATGTGCCCCCTGAGATGATGCCCACCGTCATAGATGAATACCTAGGAAGCA ACTCGGACGCACAAGCCAAATGCCAGGCGTTCCAGGAATTCATGGGTGACGTATTCATCAATGTTCCCACCGTCA GTTTTTCAAGATACCTTCGAGATTCTGGAAGCCCTGTCTTTTTCTATGAGTTCCAGCATCGACCCAGTTCTTTTG CGAAGATCAAACCTGCCTGGGTGAAGGCTGATCATGGGGCCGAGGGTGCTTTTGTGTTCGGAGGTCCCTTCCTCA TGGACGAGAGCTCCCGCCTGGCCTTTCCAGAGGCCACAGAGGAGGAGAAGCAGCTAAGCCTCACCATGATGGCCC AGTGGACCCACTTTGCCCGGACAGGGGACCCCAATAGCAAGGCTCTGCCTCCTTGGCCCCAATTCAACCAGGCGG AACAATATCTGGAGATCAACCCAGTGCCACGGGCCGGACAGAAGTTCAGGGAGGCCTGGATGCAGTTCTGGTCAG AGACGCTCCCCAGCAAGATACAACAGTGGCACCAGAAGCAGAAGAACAGGAAGGCCCAGGAGGACCTC<u>TGA</u>GGCC AGGCCTGAACCTTCTTGGCTGGGGCAAACCACTCTTCAAGTGGTGGCAGAGTCCCAGCACGGCAGCCCGCCTCTC CCCCTGCTGAGACTTTAATCTCCACCAGCCCTTAAAGTGTCGGCCGCTCTGTGACTGGAGTTATGCTCTTTTGAA ATGTCACAAGGCCGCCTCCCACCTCTGGGGCATTGTACAAGTTCTTCCCTCTCCCTGAAGTGCCTTTCCTGCTTT CCCCTCAGAGGAGCTCTCTCAAAATGGGGATTAGCCTAACCCCACTCTGTCACCCACACCAGGATCGGGTGGGA CCAGAGCCTTCAGGTGCCAAAGCCATACTCAGGCCCCCACCGACATTGTCCACCCTGGCCAGAAGGGTGCATGCC AATGGCAGAGACCTGGGATGGGAGAAGTCCTGGGGCGCCCAGGGGATCCAGCCTAGAGCAGACCTTAGCCCCTGAC TAAGGCCTCAGACTAGGGCGGGAGGGGTCTCCTCCTCTCTGCTGCCCAGTCCTGGCCCCTGCACAAGACAACAGA ATCCATCAGGGCCATGAGTGTCACCCAGACCTGACCCTCACCAATTCCAGCCCCTGACCCTCAGGACGCTGGATG CCAGCTCCCAGCCCCAGTGCCGGGTCCTCCCTCCCTTCCTGGCTTGGGGAGACCAGTTTCTGGGGAGCTTCCAAG AGCACCCACCAAGACACAGCAGGACAGGCCAGGGGAGGGCATCTGGACCAGGGCATCCGTCGGGCTATTGTCACA GAGAAAAGAAGAGACCCACCCACTCGGGCTGCAAAAGGTGAAAAGCACCAAGAGGTTTTCAGATGGAAGTGAGAG GTGACAGTGTGCTGGCAGCCCTCACAGCCCTCGCTTGCTCTCCCTGCCGCCTCTGCCTGGGCTCCCACTTTGGCA GCACTTGAGGAGCCCTTCAACCCGCCGCTGCACTGTAGGAGCCCCTTTCTGGGCTGGCCAAGGCCGGAGCCAGCT TAGCACCTGGGCCAGCAGCTGCTGTGCTCGATTTCTCGCTGGGCCTTAGCTGCCTCCCCGCGGGGCAGGGCTCGG GACCTGCAGCCCTCCATGCCTGACCCTCCCCCACCCCCGTGGGCTCCTGTGCGGCCGGAGCCTCCCCAAGGAG CGCCGCCCCTGCTCCACAGCGCCCAGTCCCATCGACCACCCAAGGGCTGAGGAGTGCGGGTGCACAGCGCGGGA CTGGCAGGCAGCTCCACCTGCTGCCCCAGTGCTGGATCCACTGGGTGAAGCCAGCTGGGCTCCTGAGTCTGGTGG GGACTTGGAGAACCTTTATGTCTAGCTAAGGGATTGTAAATACACCGATGGGCACTCTGTATCTAGCTCAAGGTT TGTAAACACACCAATCAGCACCCTGTGTCTAGCTCAGTGTTTGTGAATGCACCAATCCACACTCTGTATCTGGCT ACTCTGGTGGGGACTTGGAGAACCTTTGTGTCCACACTCTGTATCTAGCTAATCTAGTGGGGGATGTGGAGAACCT TTGTGTCTAGCTCAGGGATCGTAAACGCACCAATCAGCACCCTGTCAAAACAGACCACTTGACTCTCTGTAAAAT GGACCAATCAGCAGGATGTGGGTGGGGCGAGACAAGAGAATAAAAGCAGGCTGCCTGAGCCAGCAGTGACAACCC CCCTCGGGTCCCCTCCCACGCCGTGGAAGCTTTGTTCTTTCGCTCTTTTGCAATAAATCTTGCTACTGCCCAAAA

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FIGURE 542

MERAVRVESGVLVGVVCLLLACPATATGPEVAQPEVDTTLGRVRGRQVGVKGTDRLVNVFLGI
PFAQPPLGPDRFSAPHPAQPWEGVRDASTAPPMCLQDVESMNSSRFVLNGKQQIFSVSEDCLV
LNVYSPAEVPAGSGRPVMVWVHGGALITGAATSYDGSALAAYGDVVVVTVQYRLGVLGFFSTG
DEHAPGNQGFLDVVAALRWVQENIAPFGGDLNCVTVFGGSAGGSIISGLVLSPVAAGLFHRAI
TQSGVITTPGIIDSHPWPLAQKIANTLACSSSSPAEMVQCLQQKEGEELVLSKKLKNTIYPLT
VDGTVFPKSPKELLKEKPFHSVPFLMGVNNHEFSWLIPRGWGLLDTMEQMSREDMLAISTPVL
TSLDVPPEMMPTVIDEYLGSNSDAQAKCQAFQEFMGDVFINVPTVSFSRYLRDSGSPVFFYEF
QHRPSSFAKIKPAWVKADHGAEGAFVFGGPFLMDESSRLAFPEATEEEKQLSLTMMAQWTHFA
RTGDPNSKALPPWPQFNQAEQYLEINPVPRAGQKFREAWMQFWSETLPSKIQQWHQKQKNRKA
QEDL

Important features:

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 226-245

N-glycosylation site.

amino acids 105-109

N-myristoylation sites.

amino acids 10-16, 49-55, 62-68, 86-92, 150-156, 155-161, 162-168, 217-223, 227-233, 228-234, 232-238, 262-268, 357-363, 461-467

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 12-23

Carboxylesterases type-B serine active site.

amino acids 216-232

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FIGURE 543

 $\tt CTGGGGGGCCCCACGGCCTCTTTCCTGAGGAGCCGCCGCCGCTTAGCGTGGCCCCCAGGGACTACCTGAACCAC$ TATCCCGTGTTTGTGGGCAGCGGGCCCGGACGCCTGACCCCCGCAGAAGGTGCTGACGACCTCAACATCCAGCGA GTCCTGCGGGTCAACAGGACGCTGTTCATTGGGGACAGGGACAACCTCTACCGCGTAGAGCTGGAGCCCCCCACG TCCACGGAGCTGCGGTACCAGAGGAAGCTGACCTGGAGATCTAACCCCAGCGACATAAACGTGTGTCGGATGAAG GGCAAACAGGAGGCGAGTGTCGAAACTTCGTAAAGGTGCTCCTTCGGGACGAGTCCACGCTCTTTGTGTGC GGTTCCAACGCCTTCAACCCGGTGTGCGCCAACTACAGCATAGACACCCTGCAGCCCGTCGGAGACAACATCAGC GGTATGGCCCGCTGCCCGTACGACCCCAAGCACGCCAATGTTGCCCTCTTCTCTGACGGGATGCTCTTCACAGCT ACTGTTACCGACTTCCTAGCCATTGATGCTGTCATCTACCGCAGCCTCGGGGACAGGCCCACCCTGCGCACCGTG AAACATGACTCCAAGTGGTTCAAAGAGCCTTACTTTGTCCATGCGGTGGAGTGGGGCAGCCATGTCTACTTCTTC TTCCGGGAGATTGCGATGGAGTTTAACTACCTGGAGAAGGTGGTGGTGTCCCGCGTGGCCCGAGTGTGCAAGAAC CCCGGAGACTCCCATTTCTACTTCAACGTGCTGCAGGCTGTCACGGGCGTGGTCAGCCTCGGGGGCCCGGTG GTCCTGGCCGTTTTTTCCACGCCCAGCAACAGCATCCCTGGCTCGGCTGTCTGCCCCTTTGACCTGACACAGGTG GCAGCTGTGTTTGAAGGCCGCTTCCGAGAGCAGAAGTCCCCCGAGTCCATCTGGACGCCGGTGCCGGAGGATCAG GTGCCTCGACCCCGGCTGCTGCCGCAGCCCCCGGGATGCAGTACAATGCCTCCAGCGCCTTGCCGGATGAC ATCCTCAACTTTGTCAAGACCCACCCTCTGATGGACGAGGCGGTGCCCTCGCTGGGCCATGCGCCCTGGATCCTG CGGACCCTGATGAGGCACCAGCTGACTCGAGTGGCTGTGGACGTGGGAGCCGGCCCCTGGGGCAACCAGACCGTT GTCTTCCTGGGTTCTGAGGCGGGACGGTCCTCAAGTTCCTCGTCCGGCCCAATGCCAGCACCTCAGGGACGTCT GGGCAGCGGCTGCTGAGCTTGGAGCTGGACGCAGCTTCGGGGGGCCTGCTGGCTTCCCCCGCTGCGTGGTC CGAGTGCCTGTGGCTCCCAGCAGTACTCGGGGTGTATGAAGAACTGTATCGGCAGTCAGGACCCCTACTGC GGGTGGCCCCCGACGCTCCTGCATCTTCCTCAGCCCGGGCACCAGAGCCGCCTTTGAGCAGGACGTGTCCGGG GCCAGCACCTCAGGCTTAGGGGACTGCACAGGACTCCTGCGGGCCAGCCTCTCCGAGGACCGCGGGGGCTGGTG TCGGTGAACCTGCTGGTAACGTCGGTGGCGGCCTTCGTGGTGGGAGCCGTGGTGTCCGGCTTCAGCGTGGGC TGGTTCGTGGGCCTCCGTGAGCGGCGGGAGCTGGCCCGGCGCAAGGACAAGGACCATCCTGGCGCACGGGGCG GGCGAGGCGGTGCTGAGCGTCAGCCGCCTGGGCGAGCGCAGGGCGCAGGGTCCCGGGGGCCGGGGCGGAGGCGGT GGCGGTGGCGCCGGGGTTCCCCCGGAGGCCCTGCTGGCGCCCCTGATGCAGAACGGCTGGGCCAAGGCCACGCTG CTGCCCACTCCGCACCCCCACGCCTGGGCCCCGCGCCTGGGACCACGGCCACCCCTGCTCCCGGCC TCCGCTTCATCCTCCTCCTGCTGCTGCCGCCCGGGCCCCCGAGCAGCCCCCCGCGCCTGGGGAGCCGACC CCGGACCGCCGGCGGTGTTCCGCGCCCACGGGCCCCTTGGACCCAGCCTCAGCCGCCGATGGCCTCCCGCGG CCCTGGAGCCCGCCCCGACGGCAGCCTGAGGAGGCCACTGGGCCCCCACGCCCCTCCGGCCGCCACCCTGCGC GACTTGGCCCACCTCCTCCCCTATGGGGGGGGGGGACAGGACTGCGCCCCCGTGCCCTAGGCCGGGGGCCCCCCG ATGCCTTGGCAGTGCCAGCCACGGGAACCAGGAGCGAGAGCGGTGCCAGAACGCCGGGGCCCGGGGCAACTCCG AGTGGGTGCTCAAGTCCCCCCGCGACCCACCCGCGGAGTGGGGGGCCCCCTCCGCCACAAGGAAGCACCAG TGGGCGTGTGTCAAGTGGGCCACGCGTGCAGGGTGTGTCCACGAGCGACGATCGTGGTGGCCCCAGCGGCC TGGGCGTTGGCTGAGCCGACGCTGGGGCTTCCAGAAGGCCCGGGGGTCTCCGAGGTGCCGGTTAGGAGTTTGAAC ATACGGCCCAGGGTGGTGAGAGAGTCCCATGCCACCGTCCCCTTGTGACCTCCCCCTATGACCTCCAGCTGA CCATGCATGCCACGTGGCTGGCTCGTCTCTGCCCTCTTTGGAGTTTGCCTCCCCAGCCCCCTCCCCATCAAT

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FIGURE 544

MQTPRASPPRPALLLLLLLLGGAHGLFPEEPPPLSVAPRDYLNHYPVFVGSGPGRLTPAEGAD DLNIQRVLRVNRTLFIGDRDNLYRVELEPPTSTELRYQRKLTWRSNPSDINVCRMKGKQEGEC RNFVKVLLLRDESTLFVCGSNAFNPVCANYSIDTLQPVGDNISGMARCPYDPKHANVALFSDG MLFTATVTDFLAIDAVIYRSLGDRPTLRTVKHDSKWFKEPYFVHAVEWGSHVYFFFREIAMEF NYLEKVVVSRVARVCKNDVGGSPRVLEKQWTSFLKARLNCSVPGDSHFYFNVLQAVTGVVSLG GRPVVLAVFSTPSNSIPGSAVCAFDLTQVAAVFEGRFREQKSPESIWTPVPEDQVPRPRPGCC AAPGMQYNASSALPDDILNFVKTHPLMDEAVPSLGHAPWILRTLMRHQLTRVAVDVGAGPWGN QTVVFLGSEAGTVLKFLVRPNASTSGTSGLSVFLEEFETYRPDRCGRPGGGETGQRLLSLELD AASGGLLAAFPRCVVRVPVARCQQYSGCMKNCIGSQDPYCGWAPDGSCIFLSPGTRAAFEQDV SGASTSGLGDCTGLLRASLSEDRAGLVSVNLLVTSSVAAFVVGAVVSGFSVGWFVGLRERREL ARRKDKEAILAHGAGEAVLSVSRLGERRAQGPGGRGGGGGGGAGVPPEALLAPLMQNGWAKAT LLQGGPHDLDSGLLPTPEQTPLPQKRLPTPHPHPHALGPRAWDHGHPLLPASASSSLLLLAPA RAPEQPPAPGEPTPDGRLYAARPGRASHGDFPLTPHASPDRRRVVSAPTGPLDPASAADGLPR PWSPPTGSLRRPLGPHAPPAATLRRTHTFNSGEARPGDRHRGCHARPGTDLAHLLPYGGADR TAPPVP

Important features:

Signal peptide:

amino acids 1-25

Transmembrane domains:

amino acids 318-339, 598-617

N-glycosylation sites.

amino acids 74-78, 155-159, 167-171, 291-295, 386-390, 441-445, 462-466

Glycosaminoglycan attachment sites.

amino acids 51-55, 573-577

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 102-106

N-myristoylation sites.

amino acids 21-27, 50-56, 189-195, 333-339, 382-388, 448-454, 490-496, 491-497, 508-514, 509-515, 531-537, 558-564, 569-575, 574-580, 580-586, 610-616, 643-649, 663-669, 666-672, 667-673, 668-674, 669-675, 670-676, 868-874, 879-885

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FIGURE 545

GATGGCGCAGCCACAGCTTCTGTGAGATTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGGG GACCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGAGGCTAT**ATG**CGTCAATTCCCCAAA CCAGGCCTTACCTGCTGGGCACTAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGCCACG ACCTGTGCCACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTCACGGGAG GCTTGGCAGTTTTTCTTACTCCTGTGGTCTCCAGATTTCAGGCCTAAGATGAAAGCCTCTAGT CTTGCCTTCAGCCTTCTCTCTGCTGCGTTTTATCTCCTATGGACTCCTTCCACTGGACTGAAG ACACTCAATTTGGGAAGCTGTGTGATCGCCACAAACCTTCAGGAAATACGAAATGGATTTTCT GAGATACGGGGCAGTGTGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTAAGGAGGACT GAGTCTTTGCAAGACACAAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTTGCTAAGACTC TATCTGGACAGGGTATTTAAAAACTACCAGACCCCTGACCATTATACTCTCCGGAAGATCAGC AGCCTCGCCAATTCCTTTCTTACCATCAAGAAGGACCTCCGGCTCTCTCATGCCCACATGACA TGCCATTGTGGGGAGGAAGCAATGAAGAAATACAGCCAGATTCTGAGTCACTTTGAAAAGCTG GAGACAGAA**TAG**GAGGAAAGTGATGCTGCTGCTAAGAATATTCGAGGTCAAGAGCTCCAGTCT TCAATACCTGCAGAGGAGGCATGACCCCAAACCACCATCTCTTTACTGTACTAGTCTTGTGCT GGTCACAGTGTATCTTATTTATGCATTACTTGCTTCCTTGCATGATTGTCTTTATGCATCCCC AATCTTAATTGAGACCATACTTGTATAAGATTTTTGTAATATCTTTCTGCTATTGGATATATT AAACTTTAAAAAAATTCACAGATTATATTTATAACCTGACTAGAGCAGGTGATGTATTTTTAT ACAGTAAAAAAAAACCTTGTAAATTCTAGAAGAGTGGCTAGGGGGGTTATTCATTTGTAT TCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGATATTTGAAATTGAACCAATGAC TACTTAGGATGGGTTGTGGAATAAGTTTTGATGTGGAATTGCACATCTACCTTACAATTACTG

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FIGURE 546

MRQFPKTSFDISPEMSFSIYSLQVPAVPGLTCWALTAEPGWGQNKGATTCATNSHSDSELRPE IFSSREAWQFFLLLWSPDFRPKMKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNLQE IRNGFSEIRGSVQAKDGNIDIRILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTPDHY TLRKISSLANSFLTIKKDLRLSHAHMTCHCGEEAMKKYSQILSHFEKLEPQAAVVKALGELDI LLQWMEETE

Important features:

Signal peptide:

amino acids 1-42

cAMP- and cGMP-dependent protein kinase phosphorylation sites. amino acids 192-195, 225-228

N-myristoylation sites.

amino acids 42-47, 46-51, 136-141

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FIGURE 547

AGCAACTCAAGTTCATCATTGTCCTGAGAGAGAGGAGCAGCGCGGGTTCTCGGCCGGGACAGCA GAACGCCAGGGGACCCTCACCTGGGCGCGCGGGGCACGGGCTTTGATTGTCCTGGGGTCGCG GAGACCCGCGCCTGCCCTGCACGCCGGGCGGCAACCTTTGCAGTCGCGTTGGCTGCCGA TCGGCCGGCGGTCCCTGCCGAAGGCTCGGCTGCTTCTGTCCACCTCTTACACTTCTTCATTT ATCGGTGGATCATTTCGAGAGTCCGTCTTGTAA**ATG**TTTGGCACTTTGCTACTTTATTGCTTC TTTCTGGCGACAGTTCCAGCACTCGCCGAGACCGGCGGAGAAAGGCAGCTGAGCCCGGAGAAG CAGGCAGTGGATACATCAGGGAATAAATTCACATCTTCTCCAGGCGAAAAGGTCTTCCAGGTG AAAGTCTCAGCACCAGAGGAGCAATTCACTAGAGTTGGAGTCCAGGTTTTAGACCGAAAAGAT GGGTCCTTCATAGTAAGATACAGAATGTATGCAAGCTACAAAAATCTGAAGGTGGAAATTAAA TTCCAAGGGCAACATGTGGCCAAATCCCCATATATTTTAAAAGGGCCGGTTTACCATGAGAAC TGTGACTGTCCTCTGCAAGATAGTGCAGCCTGGCTACGGGAGATGAACTGCCCTGAAACCATT GCTCAGATTCAGAGAGATCTGGCACATTTCCCTGCTGTGGATCCAGAAAAGATTGCAGTAGAA ATCCCAAAAAGATTTGGACAGAGGCAGAGCCTATGTCACTACACCTTAAAGGATAACAAGGTT TATATCAAGACTCATGGTGAACATGTAGGTTTTAGAATTTTCATGGATGCCATACTACTTTCT TTGACTAGAAAGGTGAAGATGCCAGATGTGGAGCTCTTTGTTAATTTGGGAGACTGGCCTTTG GAAAAAAAGAAATCCAATTCAAACATCCATCCGATCTTTTCCTGGTGTGGCTCCACAGATTCC AAGGATATCGTGATGCCTACGTACGATTTGACTGATTCTGTTCTGGAAACCATGGGCCGGGTA AGTCTGGATATGATGTCCGTGCAAGCTAACACGGGTCCTCCCTGGGAAAGCAAAAATTCCACT GCCGTCTGGAGAGGCCGAGACAGCCGCAAAGAGAGACTCGAGCTGGTTAAACTCAGTAGAAAA CACCCAGAACTCATAGACGCTGCTTTCACCAACTTTTTCTTCTTTAAACACGATGAAAACCTG ATCGATGGCACTGTAGCAGCTTATCGCCTGCCATATTTGCTAGTTGGTGACAGTGTTGTGCTG AAGCAGGATTCCATCTACTATGAACATTTTTACAATGAGCTGCAGCCCTGGAAACACTACATT CCAGTTAAGAGCAACCTGAGCGATCTGCTAGAAAAACTTAAATGGGCGAAAGATCACGATGAA GAGGCCAAAAAGATAGCAAAAGCAGGACAAGAATTTGCAAGAAATAATCTCATGGGCGATGAC ATCCGAGAGGGCATGAAAAGGGTAGAACCACAGACTGAGGACGACCTCTTCCCTTGTACTTGC CATAGGAAAAAGACCAAAGATGAACTC**TGA**TATGCAAAATAACTTCTATTAGAATAATGGTGC TCTGAAGACTCTTCTTAACTAAAAAGAAGAATTTTTTTTAAGTATTAATTCCATGGACAATATA AAATCTGTGTGATTGTTTGCAGTATGAAGACACATTTCTACTTATGCAGTATTCTCATGACTG TACTTTAAAGTACATTTTTAGAATTTTATAATAAAACCACCTTTATTTTAAAGGAAAAAA

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FIGURE 548

MFGTLLLYCFFLATVPALAETGGERQLSPEKSEIWGPGLKADVVLPARYFYIQAVDTSGNKFT
SSPGEKVFQVKVSAPEEQFTRVGVQVLDRKDGSFIVRYRMYASYKNLKVEIKFQGQHVAKSPY
ILKGPVYHENCDCPLQDSAAWLREMNCPETIAQIQRDLAHFPAVDPEKIAVEIPKRFGQRQSL
CHYTLKDNKVYIKTHGEHVGFRIFMDAILLSLTRKVKMPDVELFVNLGDWPLEKKKSNSNIHP
IFSWCGSTDSKDIVMPTYDLTDSVLETMGRVSLDMMSVQANTGPPWESKNSTAVWRGRDSRKE
RLELVKLSRKHPELIDAAFTNFFFFKHDENLYGPIVKHISFFDFFKHKYQINIDGTVAAYRLP
YLLVGDSVVLKQDSIYYEHFYNELQPWKHYIPVKSNLSDLLEKLKWAKDHDEEAKKIAKAGQE
FARNNLMGDDIFCYYFKLFQEYANLQVSEPQIREGMKRVEPQTEDDLFPCTCHRKKTKDEL

Important features:

Signal peptide:

amino acids 1-17

N-glycosylation sites.

amino acids 302-306, 414-418

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 243-247, 495-499

Tyrosine kinase phosphorylation site.

amino acids 341-348

N-myristoylation sites.

amino acids 59-65, 118-124, 184-190, 258-264, 370-376, 439-445

Endoplasmic reticulum targeting sequence.

amino acids 499-504

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FIGURE 549

GGGTGATTGAACTAAACCTTCGCCGCACCGAGTTTGCAGTACGGCCGTCACCCGCACCGCTGC CTGCTTGCGGTTGGAGAAATCAAGGCCCTACCGGGCCTCCGTAGTCACCTCTCTATAGTGGGC GTGGCCGAGGCCGGGGTGACCCTGCCGGAGCCTCCGCTGCCAGCGACATGTTCAAGGTAATTC AGAGGTCCGTGGGGCCAGCCTGAGCTTGCTCACCTTCAAAGTCTATGCAGCACCAAAAA AGGACTCACCTCCCAAAAATTCCGTGAAGGTTGATGAGCTTTCACTCTACTCAGTTCCTGAGG GTCAATCGAAGTATGTGGAGGAGGCAAGGAGCCAGCTTGAAGAAAGCATCTCACAGCTCCGAC ACTATTGCGAGCCATACACAACCTGGTGTCAGGAAACGTACTCCCAAACTAAGCCCAAGATGC AAAGTTTGGTTCAATGGGGGTTAGACAGCTATGACTATCTCCAAAATGCACCTCCTGGATTTT TTCCGAGACTTGGTGTTATTGGTTTTGCTGGCCTTATTGGACTCCTTTTGGCTAGAGGTTCAA AACAAGCCATCGTGTTTGCCCAGGTCAGTGGGGAGAGATTATATGACTGGGGTTTACGAGGAT ATATAGTCATAGAAGATTTGTGGAAGGAGAACTTTCAAAAGCCAGGAAATGTGAAGAATTCAC CTGGAACTAAG**TAG**AAAACTCCATGCTCTGCCATCTTAATCAGTTATAGGTAAACATTGGAAA CTCCATAGAATAAATCAGTATTTCTACAGAAAAATGGCATAGAAGTCAGTATTGAATGTATTA AATTGGCTTTCTTCAGGAAAAACTAGACCAGACCTCTGTTATCTTCTGTGAAATCATCCT ACAAGCAAACTAACCTGGAATCCCTTCACCTAGAGATAATGTACAAGCCTTAGAACTCCTCAT AAAAAAAAAAAAA

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FIGURE 550

MFKVIQRSVGPASLSLLTFKVYAAPKKDSPPKNSVKVDELSLYSVPEGQSKYVEEARSQLEES ISQLRHYCEPYTTWCQETYSQTKPKMQSLVQWGLDSYDYLQNAPPGFFPRLGVIGFAGLIGLL LARGSKIKKLVYPPGFMGLAASLYYPQQAIVFAQVSGERLYDWGLRGYIVIEDLWKENFQKPG NVKNSPGTK

Important features:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 111-130

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 26-30

Tyrosine kinase phosphorylation site:

Amino acids 36-44

N-myristoylation sites:

Amino acids 124-130;144-150;189-195

(19) World Intellectual Property Organization International Bureau





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(54) Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 53-57

(57) Abstract: The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides.

Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.





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PCT/US00/06884	15 March 2000 (15.03.2000)	US
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PCT/US00/14941	30 May 2000 (30.05.2000)	US
PCT/US00/15264	2 June 2000 (02.06.2000)	US
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60/000.000	15 September 2000 (15.09.2000)	US
PCT/US00/30952		
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Inte: anal Application No PC I/US 00/32678

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/47 C12N15/62 C07K16/18 C07K14/705 C12Q1/68 CO7K16/28 G01N33/53 A61K38/17 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) I PC 7 C12N C07K G01N A61K C12Q Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category 1-20. WO 98 21328 A (KATO SEISHI ; PROTEGENE INC X (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 69-71 22 May 1998 (1998-05-22)
* see seq.ID's.12, 37 and 62: clone
HP10122 * 1-20 WO 99 09061 A (GENETICS INST) X 25 February 1999 (1999-02-25) * see clone am910_li * -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. X Special categories of cited documents: T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 1 2. 11. m 8 August 2001 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Smalt, R Fax: (+31-70) 340-3016

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Inter: nal Application No
PC1/US 00/32678

	PC1/US 00/32678	
ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
IWAMURO SHAWICHI ET AL: "Multi-ubiquitination of a nascent membrane protein produced in a rabbit reticulocyte lysate." JOURNAL OF BIOCHEMISTRY (TOKYO), vol. 126, no. 1, July 1999 (1999-07), pages 48-53, XP002174228 ISSN: 0021-924X the whole document	1-20	
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KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document		
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national application No. PCT/US 00/32678

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
з. 🗌	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box il	Observations where unity of Invention is lacking (Continuation of item 2 of first sheet)
This Inte	rnational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. 🗶	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-20 and 69-71, all partially
Remark	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-20 and 69-71, all partially

PR0177: nucleic acid with seq.ID.1, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.2 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.2 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide.

Inventions 2-242: claims 1-20 and 69-71,
 all partially

Subject matter as defined for invention 1, but related to the respective nucleic acid/polypeptide sequences of: Invention 2: PRO3574, represented by seq.ID.s 3 and 4, Invention 3: PR01280, represented by seq.ID.s 5 and 6, Invention 4: PRO4984, represented by seq.ID's 7 and 8. Invention 15: PR01471, represented by seq.ID.s 29 and 30, (PR01114 skipped; follows below) Invention 16: PRO1076, represented by seq.ID.s 33 and 34, ... Invention 92: PRO4345, represented by seq.ID.s 185 and 186, (PRO4978 skipped; follows below) Invention 93: PRO4327, represented by seq.ID.s 221 and 222, Invention 107: PR06028, represented by seq.ID.s 217 and 218, (PRO100 skipped; follows below) Invention 108: PRO4327, represented by seq.ID.s 221 and 222, Invention 132: PR0197, represented by seg.ID.s 269 and 270. (PR0195 skipped; follows below) Invention 133: PR0187, represented by seq.ID.s 273 and 274, (PR0182 skipped: follows below) Invention 134: PR0188, represented by seq.ID.s 277 and 278, Invention 136: PR0184, represented by seq.ID.s 281 and 282, (PR0185 skipped: follows below) Invention 137: PRO200, represented by seq.ID.s 285 and 286, (PR0202 skipped: follows below) Invention 138: PRO214, represented by seq.ID.s 289 and 290, (PRO215 skipped: follows below) Invention 139: PRO219, represented by seq.ID.s 293 and 294, (PRO211 skipped: follows below) Invention 140: PR0220, represented by seq.ID.s 297 and 298. (PRO366, PRO216, PRO221 skipped: follows below) Invention 141: PRO228, represented by seq.ID.s 305 and 306,

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(PRO217, PRO222, PRO224 skipped: follows below)
Invention 142: PRO230, represented by seq.ID.s 313 and 314,
(PRO198 skipped: follows below)
Invention 143: PRO226, represented by seq.ID.s 317 and 318,
Invention 151: PRO323, represented by seq.ID.s 333 and 334,
(PRO245 skipped: follows below)
Invention 152: PRO246, represented by seq.ID.s 337 and 338,
Invention 155: PRO257, represented by seq.ID.s 343 and 344,
(PRO172 skipped: follows below)
Invention 156: PRO258, represented by seq.ID.s 347 and 348,
(PRO265 skipped: follows below)
Invention 157: PRO326, represented by seq.ID.s 351 and 352,
(PRO266 skipped: follows below)
Invention 158: PRO269, represented by seq.ID.s 355 and 356,
Invention 160: PR0328, represented by seq.ID.s 359 and 360,
(PRO344 skipped: follows below)
Invention 161: PRO272, represented by seq.ID.s 363 and 364.
(PRO301 skipped: follows below)
Invention 162: PRO331, represented by seq.ID.s 367 and 368.
Invention 165: PRO310, represented by seq.ID.s 373 and 374,
(PRO337 skipped: follows below)
Invention 166: PRO346, represented by seq.ID.s 377 and 378,
Invention 167: PRO350, represented by seq.ID.s 379 and 380,
(PRO526 skipped: follows below)
Invention 168: PRO381, represented by seq.ID.s 383 and 384,
Invention 173: PRO731, represented by seq.ID.s 393 and 394,
(PRO322 skipped: follows below)
Invention 174: PR0536, represented by seq.ID.s 397 and 398.
(PR0719 skipped: follows below)
Invention 175: PR0619, represented by seq.ID.s 401 and 402.
Invention 214: PR01475, represented by seq.ID.s 479 and 480.
(PRO1312 skipped: follows below)
Invention 215: PR01308, represented by seq.ID.s 483 and 484,
Invention 222: PR01358, represented by seq.ID.s 497 and 498,
(PR01286 skipped: follows below)
Invention 223: PR01294, represented by seq.ID.s 501 and 502,
Invention 224: PR01273, represented by seq.ID.s 503 and 504,
(PR01279 skipped: follows below)
Invention 225: PR01195, represented by seq.ID.s 507 and 508,
Invention 226: PR01271, represented by seq.ID.s 509 and 510,
(PRO1338, PRO1343 skipped: follows below)
Invention 227: PR01434, represented by seq.ID.s 513 and 514,
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Invention 237: PR01693, represented by seq.ID.s 536 and 537,

(PR01868 skipped: follows below)

Invention 238: PRO1890, represented by seq.ID.s 539 and 540.

Invention 240: PRO4353, represented by seq.ID.s 543 and 544, (PRO1801 skipped: follows below)

Invention 241: PRO4357, represented by seq.ID.s 547 and 548, Invention 242: PRO4302, represented by seq.ID.s 549 and 550.

For the sake of conciseness, the first subject matter is explicitly defined, the subject matter of inventions 2-241 are defined by analogy thereto, whereby the numbering of the

sequences is followed, except for sequences which are mentioned in one of claims 21-68; inventions relating thereto follow below.

Invention 243: claims 43-49, 53, 54 completely,
 and claims 1-24, 29-31, 35, 36, 69-71,
 all partially

PRO1114: nucleic acid with seq.ID.31, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.32 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.32 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 and/or PRO100 using their interactions with PRO1114, method for linking a bioactive molecule to a cell expressing PRO1801 and/or PRO100 through the use of PRO1114, and method of modulating at least one activity of said cell thereby.

Invention 244: claims 1-24, 29-31, 35, 36, 53, 54, 69-71, all partially

PRO4978: nucleic acid with seq.ID.187, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.188 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.188 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 using its interaction with PRO4978, method for linking a bioactive molecule to a cell expressing PRO1801 through the use of

PRO4978, and method of modulating at least one activity of said cell thereby.

Invention 245: claims 39-42, 50-52, 55,
56 completely, and claims 1-20, 69-71,
all partially

PRO100: nucleic acid with seq.ID.219, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.220 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.220 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 and/or PRO1114 using their interactions with PRO100, method for linking a bioactive molecule to a cell expressing PRO1801 and/or PRO1114 through the use of PRO100, and method of modulating at least one activity of said cell thereby.

Invention 246: claims 1-20, 57, 69-71,
 all partially

PRO195: nucleic acid with seq.ID.271, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.272 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.272 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO195 protein.

Invention 247: claim 66 completely, and claims 1-20, 58, 59, 69-71, all partially

PRO182: nucleic acid with seq.ID.275, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.276 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.276 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of

said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for inhibiting the binding of A-peptide to factor VIIA using the PR0182 protein.

Invention 248: claims 1-20, 67, 69-71,
 all partially

PRO185: nucleic acid with seq.ID.283, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.284 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.284 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for inhibiting the differentiation of adipocytes using the PRO185 protein.

Invention 249: claims 1-20, 57, 59, 60, 69-71,
 all partially

PRO202: nucleic acid with seq.ID.287, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.288 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.288 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for stimulating the proliferation or differentiation of chondrocytes, and method for modulating the uptake of glucose or FFA by adipocytes using the PRO202 protein.

Invention 250: claims 1-20, 57, 69-71,
 all partially

PRO215: nucleic acid with seq.ID.291, encoding a polypeptide comprising the amino acid sequence as represented in

seq.ID.292 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.292 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO215 protein.

Invention 251: claims 1-20, 60, 69-71, all partially

PRO211: nucleic acid with seq.ID.295, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.296 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.296 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by adipocytes using the PRO211 protein.

Invention 252: claim 61 completely, and claims 1-20, 58, 59, 69-71, all partially

PR0366: nucleic acid with seq.ID.299, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.300 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.300 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for stimulating the proliferation of gene expression in pericytes using the PR0366 protein.

Invention 253: claim 62 completely,
 and claims 1-20, 69-71, all partially

PRO216: nucleic acid with seq.ID.301, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.302 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.302 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stilulating the release of proteoglycans from cartilage using the PRO216 protein.

Invention 254: claims 1-20, 57, 69-71, all partially

PRO221: nucleic acid with seq.ID.303, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.304 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.304 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO221 protein.

Invention 255: claims 1-20, 69-71, all partially

PRO217: nucleic acid with seq.ID.307, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.308 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.308 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO217 protein.

Invention 256: claim 68 completeley,
 and claims 1-20, 69-71, all partially

PRO222: nucleic acid with seq.ID.309, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.310 or a nucleic acid having at least 80% homology

thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.310 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for stimulating the proliferation of endothelial cells using the PRO222 protein.

Invention 257: claims 1-20, 59, 69-71,
 all partially

PRO224: nucleic acid with seq.ID.311, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.312 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.312 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for stimukating the proliferation or differentiation of chondrocytes using the PRO224 protein.

Invention 258: claims 1-20, 57-59, 67, 69-71, all partially

PR0198: nucleic acid with seq.ID.315, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.316 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.316 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for inhibiting the differentiation of adipocytes using the PR0198 protein.

Invention 259: claims 1-20, 57, 69-71,

all partially

PRO245: nucleic acid with seq.ID.335, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.336 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.336 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO245 protein.

Invention 260: claim 63 completely,
 and claims 1-20, 57-59 69-71, all partially

PR0172: nucleic acid with seq.ID.345, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.346 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.346 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for stimulating the proliferation of inner ear utricular supporting cells using the PR0172 protein.

Invention 261: claims 1-20, 57, 69-71,
 all partially

PRO265: nucleic acid with seq.ID.349, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.350 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.350 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO265 protein.

Invention 262: claims 1-20, 57, 69-71,
 all partially

PRO266: nucleic acid with seq.ID.353, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.354 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.354 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of INF-alpha from human blood using the PRO266 protein.

Invention 263: claim 64 completely, and claims 1-20, 57, 60, 69-71, all partially

PRO344: nucleic acid with seq.ID.361, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.362 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.362 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by adipocytes, and method for stimulating the proliferation of T-lymphocytes using the PRO344 protein.

Invention 264: claims 1-20, 59, 69-71, all partially

PRO301: nucleic acid with seq.ID.365, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.366 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.366 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation

or differentiation of chondrocytes using the PRO301 protein.

Invention 265: claims 1-20, 57, 69-71,
 all partially

PRO337: nucleic acid with seq.ID.375, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.376 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.376 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO337 protein.

Invention 266: claims 1-20, 65, 69-71,
 all partially

PRO526: nucleic acid with seq.ID.381, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.382 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.382 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of a cytokine from PBMC cells using the PRO526 protein.

Invention 267: claims 1-20, 57, 69-71,
 all partially

PRO322: nucleic acid with seq.ID.395, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.396 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.396 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO322 protein.

Invention 268: claims 1-20, 58, 69-71, all partially

PR0719: nucleic acid with seq.ID.399, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.400 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.400 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells using the PR0719 protein.

Invention 269: claims 1-20, 59, 69-71,
 all partially

PRO1312: nucleic acid with seq.ID.481, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.482 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.482 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation or differentiation of chondrocytes using the PRO1312 protein.

. Invention 270: claims 1-20, 57, 69-71, all partially

PRO1286: nucleic acid with seq.ID.499, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.501 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.501 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO1286 protein.

Invention 271: claims 1-20, 57, 69-71,
 all partially

PRO1279: nucleic acid with seq.ID.505, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.506 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.506 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PR01279 protein.

Invention 272: claims 1-20, 57, 60, 69-71, all partially

PRO1338: nucleic acid with seq.ID.511, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.512 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.512 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for modulating the uptake of glucose or FFA by adipocytes using the PRO1338 protein.

Invention 273: claims 1-20, 57, 65, 69-71,
 all partially

PRO1343: nucleic acid with seq.ID.513, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.514 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.514 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of

TNF-alpha from human blood, and method for stimulating the release of a cytokine from PBMC cells using the PR01343 protein.

Invention 274: claims 1-20, 59, 69-71, all partially

PRO1868: nucleic acid with seq.ID.537, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.538 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.538 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation or differentiation of chondrocytes using the PRO1868 protein.

Invention 275: claims 25-28, 32-34, 37,
 38 completely, and claims 1-20, 69-71,
 all partially

PRO1801: nucleic acid with seq.ID.545, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.546 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.546 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1114 and/or PRO4978 using its interaction with PRO1801, method for linking a bioactive molecule to a cell expressing PRO4978 and/or PRO1114 through the use of PRO1801, and method of modulating at least one activity of said cell thereby.

formation on patent family members

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